VOLUME 53 NUMBER 3

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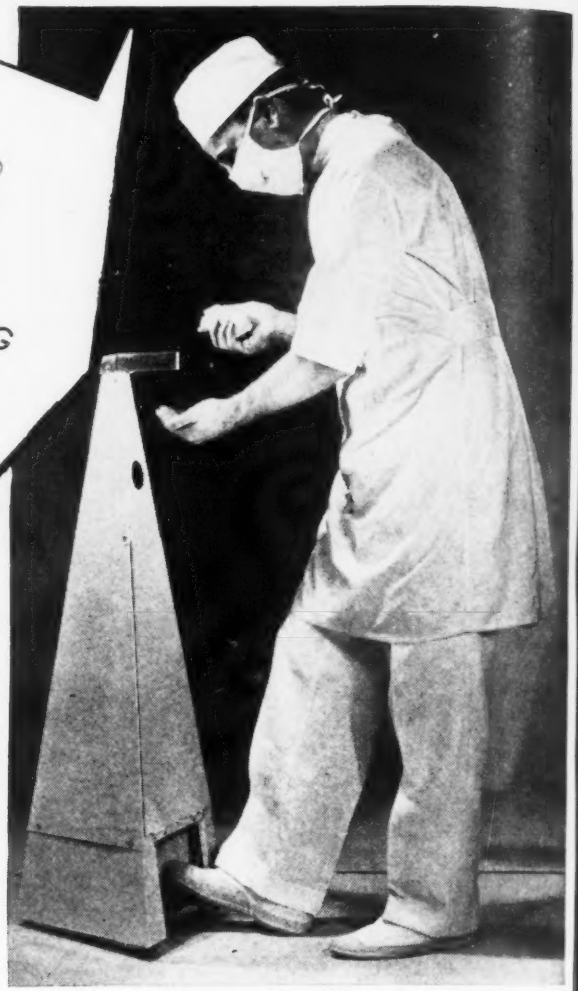

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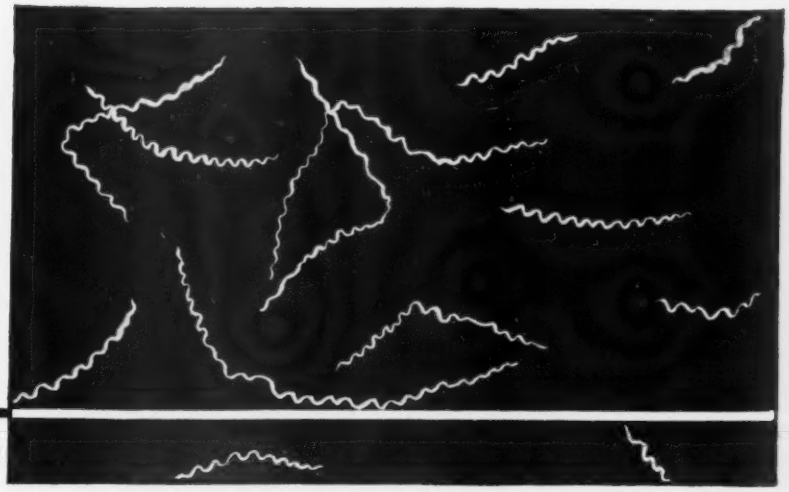

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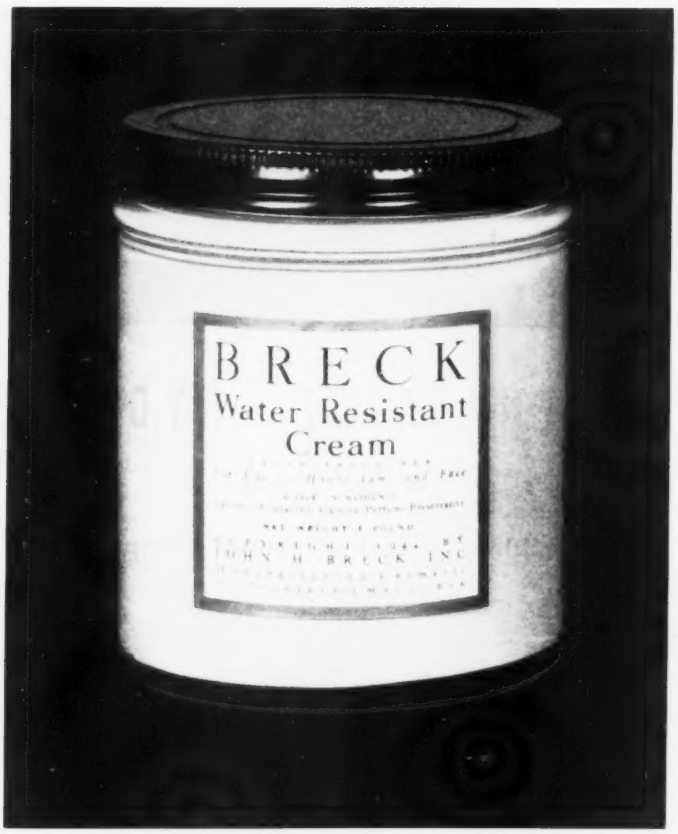

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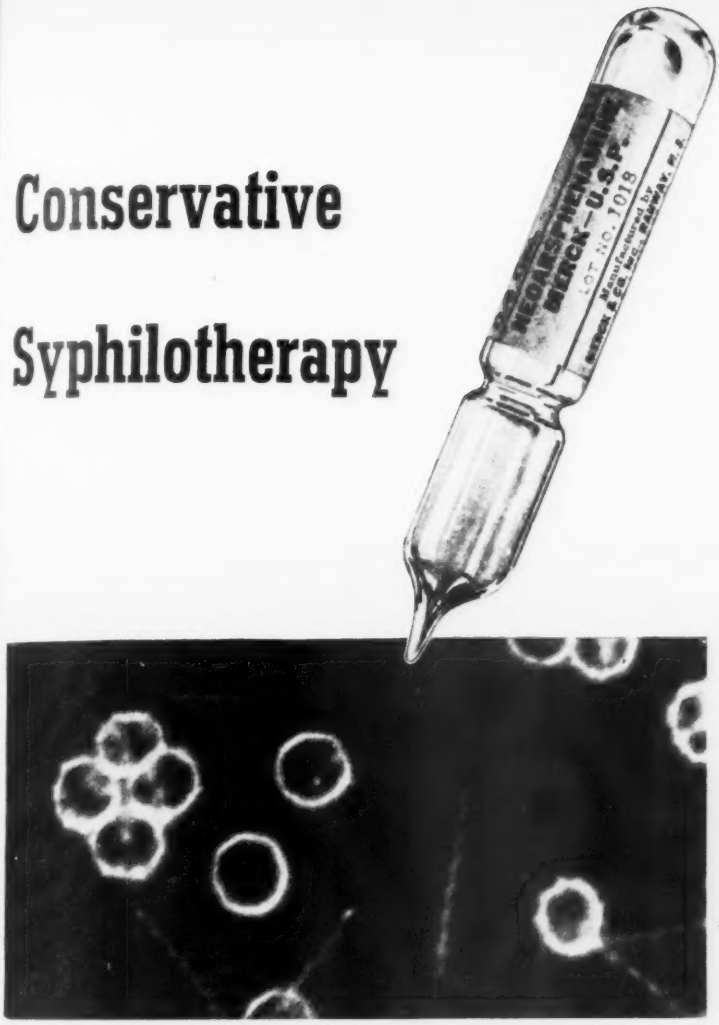

Treponema pallidum: unretouched photomicrograph of fresh human chancre exudate, under dark-field illumination; some red blood cells apparent.

THE statistical studies of Padget* have been of considerable value in establishing the need for treating primary syphilis during the seronegative stage. Under the best conditions obtainable, the syphilitic patient has less chance of being cured when treatment is delayed until the blood becomes seropositive than he has if therapy is instituted while it still is seronegative. Furthermore, the incidence of neurosyphilis has been found to be more than twice as high in seropositive primary syphilis cases than in any other.

The first three months of treatment are most important in preventing future relapse. Negative serologic reactions do not necessarily indicate noninfectiousness; hence, patients should not be permitted to relax precautions or suspend therapy until the proper number of alternating, uninterrupted courses of Neoarsphenamine Merck and Bismuth Subsalicylate have been given.

**Padget, P., Long-term results in treatment of early syphilis, J. A. M. A. 116:7-11, 1941.*

The conservative method of treating early syphilis requires the continuous administration of alternate courses of an arsenical, such as Neoarsphenamine Merck, and Bismuth, according to specific schedules. The prevention of infectious relapse largely depends on two important factors:

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[1] U.S. Nav. M. Bull. 45:783, 1945, and previous annual Navy reports.

[2] Stokes, J.H., Beerman, H. and Ingraham, N.R.: Modern Clinical Syphilology, ed. 3, Philadelphia, W.B. Saunders Company, 1945, pp. 359, 300.

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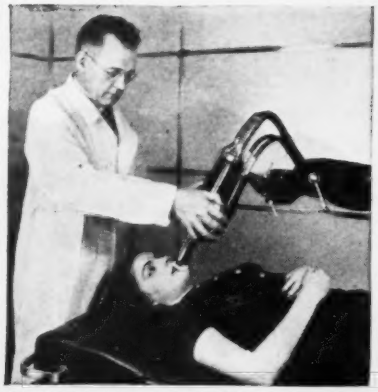

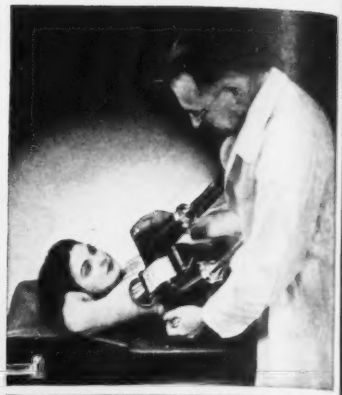

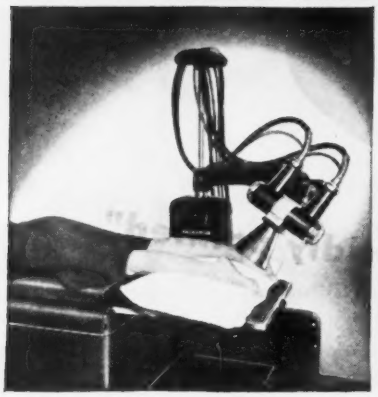

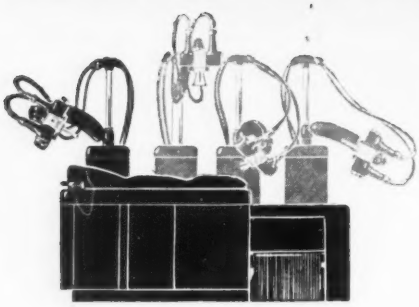

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Archives of Dermatology and Syphilology

VOLUME 53 MARCH 1946 NUMBER 3

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DERMATOPHYTOSIS AND OTHER FORMS OF INTERTRIGINOUS DERMATITIS OF THE FEET

A Comparison of Therapeutic Methods

FRED D. WEIDMAN, M.D.
PHILADELPHIA
AND
FREDERIC A. GLASS, M.D.
BALTIMORE

BOTH in civil life and in the armed forces, the control of those conditions of the feet which are commonly diagnosed as "dermatophytosis" has long been a problem. Even when "cured" they are likely to recur. They sometimes incapacitate. The incidence in college students is 50 to 70 per cent. Youth, hot climates and sweaty feet are predisposing factors. Today, in the army and navy, 8 per cent of hospital admissions in the United States are for dermatoses in general, and dermatophytosis ranks in incidence second only to contact dermatitis. In the foreign field the figure would doubtless be larger, and reports from the South Pacific area indicate that these dermatoses are outstandingly severe there. In short, there is acute need for a satisfactory means for keeping the feet of fighting men in good condition, in which connection intertriginous dermatitis poses a large problem.

At this point it is fitting to explain the relationship between "dermatophytosis" and "intertriginous dermatitis" mentioned in the foregoing paragraph. For a long time, some physicians have been jumping to the conclusion that intertriginous conditions of the toes, whether associated with lesions elsewhere on the feet or not, were due to fungous infection and were therefore dermatophytosis. This position was taken in spite of the fact that it was common knowledge that the fungi could not be demonstrated in many of the cases. One of us (F. D. W.) pointed out as far back as 1927 [1] that it was not reasonable that only fungi could cause intertrigo of the toes, and Mitchell [2] followed this up with an attempt to distinguish the cases of bacterial origin by clinical

From the Laboratory of Dermatological Research, University of Pennsylvania, assisted by a grant from the Council on Pharmacy and Chemistry, American Medical Association.

1. Weidman, F. D.: Laboratory Aspects of Dermatophytosis, Arch. Dermat. & Syph. **15**:415 (April) 1927.

2. Mitchell, J. H.: Streptococcic Infection Simulating Ringworm of the Hands and Feet, J. A. M. A. **104**:1220 (April 6) 1935.

signs. Recently, Hopkins and collaborators [3] have enlarged the idea. They found that fungi could not be demonstrated in 30 per cent of their cases, even after repeated tests, and concluded on clinical grounds that dermatoses of the feet could be caused by hypostasis, minor trauma and sweatiness in addition to the bacteria and fungi. In short, only part of the intertriginous types of dermatitis are dermatophytosis. This indicates that physicians must be more discriminating if they would exhaustively evaluate dermatitis of the feet, at least when they enjoy the facilities (including laboratory) of civilian practice and military hospitals. In the field, of course, it may be different. The cases in which the condition is due to trauma, hypostasis and sweatiness will be the more readily identified; it is those due to bacteria that pose a real problem.

It was with the full realization of the foregoing facts that we planned our studies at a penitentiary. However, with our immediate interests related to the armed forces in the field, we did not attempt to discriminate among mycotic, bacterial and other intertrigoes. We did exclude certain nonintertriginous conditions, such as callositas and the sodden placques due to sweatiness to which Hopkins and collaborators [3] have called attention. We included only those types of dermatitis which were conceivably due to bacteria or to fungi, especially if intertriginous; when there were lesions elsewhere which were of the nature of dermatophytosis, such as tinea cruris, they were included in the problem. Nor did we attempt to differentiate rigidly between dermatophytosis and bacterial disease. We adopted this policy because in the field the need is for a more or less blanket form of treatment, and, fortunately, a number of chemicals are available which are both antibacterial and antimycotic. Incidentally, the same statements hold true in much of civilian practice.

It is true that we conducted certain laboratory examinations, but they were only secondary to the larger purpose just indicated, treatment in the field. They were made for what they might be worth later. Thus, with scrapings available immediately and a rather full clinical picture in the record, the two might be found useful during the final analyses and prove to have significance with regard to some one of the therapeutic agents that we had employed. Some of the results of these laboratory examinations will be discussed later in this paper; others will be reported more fully in further communications.

The management of intertriginous infections as a whole resolves itself under three heads: (1) prophylaxis, (2) treatment under close

3. Hopkins, J. G.; Hillegas, A. B.; Camp, E.; Ledin, R. B., and Rebell, G.: Treatment and Prevention of Dermatophytosis and Related Conditions, Bull. U. S. Army M. Dept., June 1944, no. 77, p. 42.

medical supervision in a hospital and (3) treatment without such supervision. As prophylactics, dusting powders containing boric acid, with or without salicylic acid, are the mainstays, but they are not invariably effective even when prescribed with directions for regular and conscientious use. Youth, by and large, is not likely to be systematic or conscientious, either to itself or to others, concerning the feet. It must be granted that foot baths containing sodium thiosulfate or sodium hypochlorite are theoretically indicated, but they are practical only in fixed quarters, such as cantonments and institutions, and even under such conditions there is a controversy as to their usefulness. In fact, certain controlled tests made recently in an industrial plant [4] throw grave doubt on their value. As to specific curative agents, dissatisfaction is general, particularly in respect to the recurrences that are so notorious. Thus far, salicylic acid, iodine and chrysarobin are the anchors, but the last two, particularly chrysarobin, are capable of producing a chemical dermatitis and hence should be employed only under expert medical supervision.

MATERIALS AND METHODS

With dermatophytosis as ubiquitous as it is, we confined our studies to prophylaxis and to treatment without close medical supervision in a hospital, indicated as points 1 and 3 in the preceding paragraph. Certainly, these aspects of treatment are most commanding both in the armed forces and in civil life; the great majority of infections are self treated until they force the patient to consult a physician. Medicaments were therefore selected that promised no untoward reactions when employed in the absence of close medical supervision. We were fortunate in our access to a penitentiary, because patients were under excellent control and available for follow-up study.

Conditions of Tests.—The studies were begun in November 1942 and continued into the late spring of 1943. That is, we were dealing with the "winter type" of infection, such as is commonest in the population at large regardless of season. Part of the buildings of the penitentiary are one hundred or more years old. Some of the floors of cells and corridors are wooden, but most of such floors have been replaced by stone or concrete. Bathrooms are spacious, with floors partly covered by wooden gratings. The entire institution is kept scrupulously clean and has adequate medical quarters and an excellent staff. Almost all the laundering is done by each inmate for himself in his cell, with the result that even though stockings are not thoroughly sterilized in the laundry there is little likelihood that fungus is trans-

4. Peck, S. M.; Botvinick, I., and Schwartz, L.: Dermatophytosis in Industry, Arch. Dermat. & Syph. **50**:170 (Sept.) 1944.

mitted from patient to patient through stockings. Incidentally, we analyzed and compared the cases of infections originating in quarters having wooden, cement and stone floors, and we found no significant differences in relation to the various aspects of these intertriginous infections.

The inmates, all men, are largely "lifers," with an average age of 35 years. Of the group, 23.1 per cent are Negroes. There are not any requirements as to frequency of bathing; from the condition of their feet it appears that the subjects' hygiene is comparable to the average for the middle and lower classes of society. Naturally, we have checked carefully in respect to the credibility of the histories that have been given and have accepted or discounted each one pro re nata.

Records were kept on mimeographed protocols which included a diagram of the feet; on the latter, details as to the lesions were plotted. For the sake of uniformity, readings were made by one of us (F. D. W.) throughout, supplemented by conference with the other (F. A. G.) when it appeared advisable to check. In short, every effort was made to maintain uniformity in methods and standards of clinical readings. The necessity for such care cannot be overemphasized; obviously, the clinical observer who is dealing with scores of lesions cannot remember the multitudinous changes that occur over a period of weeks and months. We adopted a system of symbols for indicating the position, extent and type of lesion; these were plotted on the diagram. By the use of different-colored pencils in recording the symbols, the time factor was satisfactorily represented. By these means, a good perspective was secured, even months afterward, of the changes in the lesions, including the chronology.

Cultures were made for nearly all of the patients in order to learn later whether the species of fungus played any significant role in the premises. Scrapings were not examined under the microscope because the studies were directed primarily at the clinical aspects. The etiologic agent was important for the purposes of our study only in respect to the species (i. e., whether it was Trichophyton interdigitale or Trichophyton purpureum), a fact which cannot be determined by direct microscopic examination.

Medicaments.—Six forms of medicaments were selected for trial. Two, Cresatin-Sulzberger and zephiran chloride are accepted as disinfectants by the Council on Pharmacy and Chemistry of the American Medical Association. Pomeio and Iodolate have not been thus approved. Ointment of benzoic and salicylic acid N. F. was included as a more or less "standard" therapeutic agent for dermatophytosis—that is, as a base line for comparison of results. A foot powder, 5 per cent boric acid in powdered talc, was selected as an additional "control," as we thought at first. However, we were agreeably surprised to learn

that it had high medicinal value and, accordingly, did not serve as the control anticipated. Fortunately, though, two of the six substances (Pomeio and zephiran chloride) eventuated as controls, because the lesions treated by them were not recognizably modified; they appeared to be inert.

Description of Forms of Treatment.—Patients under all plans of therapy were instructed to keep their feet clean and dry. The following six medicaments were employed as follows:

1. Cresatin-Sulzberger is metacresylacetate, manufactured by Sharpe and Dohme, Inc., Philadelphia. It is a colorless liquid, soluble in oils and alcohol but not in water. It has a strong odor resembling that of cresol. It was used full strength once or twice daily; in the case of the interdigital spaces, on a pledget of lamb's wool. We were led to the inclusion of this fungicide in our study because otologists had found it highly successful in treatment of otomycosis.

2. Boric acid foot powder. This consisted of 5 per cent boric acid in powdered talc. Incidentally, the army issue foot powder consists of salicylic acid 2 parts, boric acid 6 parts, zinc stearate 3 parts, exsiccated alum 1 part, starch 10 parts and powdered talc 78. It was dusted onto the feet three times a week.

3. Ointment of benzoic and salicylic acid N. F. A modified stock preparation of the penitentiary was employed (3 per cent salicylic acid and 12 per cent benzoic acid, with petrolatum as the base). It was rubbed in night and morning.

4. Iodolate (iodocholeate) was employed in a 20 per cent ointment as supplied by the manufacturer. It was applied night and morning. It is manufactured by Iodocholeate Products Corporation, Newark, N. J. It is brown and smells strongly of iodine.

5. Pomeio, manufactured by the Anderson-Stolz Corporation, Kansas City, Mo., is potassium mercuric iodide and was supplied by them in 1.2 per cent aqueous solution. It is colorless and odorless and contains enough alkali (2.5 per cent sodium hydroxide) to make it slippery to the touch. It was applied in the same manner as Cresatin.

6. Zephiran chloride is a water-clear, odorless liquid made by the Winthrop Chemical Co., New York. It is a mixture of alkyl dimethyl benzyl ammonium chlorides. It was used in 1 per cent aqueous solution in the manner described for Cresatin.

All the medicaments were applied by the prisoners themselves in their cells, assisted by mimeographed sheets of instruction. We inquired at each visit whether the treatment prescribed was being adhered to. If it was not, the patient was dropped from the study. In short, we did our best to have conditions in the penitentiary parallel those in private practice.

Treatment was not instituted until enough patients (117) had been assembled who were suitable as test objects and whose cultures had been identified. These were divided into 6 groups of 20, more or less—one group for each form of treatment. Subsequent defections of patients were made good by patients with comparably severe erup-

tions who became available later. Each group was reasonably uniformly composed in respect to kinds of lesions; that is, it contained similar numbers with "mild," "moderate" and "severe" eruptions, together with representatives of T. interdigitale and T. purpureum infection. These will be referred to as "original" tests. When it became clear (in two to three weeks) that Cresatin and the boric acid powder surpassed the other forms of treatment, we confined further tests largely to these two medicaments (patients were transferred from the groups treated with zephiran, Pomeio and the others). These further tests will be designated as "supplementary" tests. This explains why the results recorded herein concern a far greater number of experiences with these two medicaments than with the others, and why "experiences" ("original" plus "supplementary" tests) far outnumber the total number of patients in the entire series.

RESULTS

Under the heading of "Results" we feel justified in submitting certain (correlated) observations other than those immediately concerning treatment—namely, the role of the age of the patient, race and others. The patients were under such excellent control that the resulting data had unusual significance and merit recording. The breakdown appears in the following paragraphs. Throughout, it should be remembered that we were dealing with winter infections. The results which immediately concern the forms of treatment will be recorded first; thereafter the "correlated" findings will be dealt with.

Evaluation of Medicaments.—Cresatin: At the outset 24 patients were tested ("original tests" in the table); the eruptions of 9 patients were cured, of 1 nearly cured and of 7 improved; 7 were stationary, and none was worse. There were not any complaints about the odor; we always inquired specifically on this point, but we realize that our clientele was not a fully representative cross section of American society. Incidentally, improvement was noted in 13 patients within a short time—namely two to three weeks; for others a period of four months was required. When the therapeutic response of patients receiving other forms of treatment, such as Pomeio and Iodolate, was found to be unsatisfactory, some of the patients were transferred to the group receiving treatment with Cresatin—45 in all. This created a supplementary group of therapeutic tests, but still within the original 117 patients. Of these, 7 were cured, 6 nearly cured, 21 improved, 9 stationary and 2 worse. The combined results of the 69 original and supplementary experiences with Cresatin were: 16 cured, 7 nearly cured, 28 improved, 16 stationary and 2 worse. The table indicates these results, together with percentages. There was only one untoward

reaction, it appears; late in the course of treatment the patient stated that the substance burned him. We could not examine him until one month later and could not check his statement objectively. In short, Cresatin made an excellent showing.

Boric Acid Powder: For the sake of brevity, we designated this "hygienic" treatment. Twenty patients were tested at the outset (original tests in the table), and, as in the case of Cresatin, a second group (supplementary experiences) was also tested as the result of transfers from other forms of treatment. The results were as follows: In the "original" group, 6 patients were cured, 3 nearly cured, 1 improved, 7 stationary and 3 worse. Ten of the 20 were at least improved after two or three weeks. In the "supplementary" group (29 in all), 10 were cured, 1 nearly cured, 12 improved, 5 stationary and 1 worse. The combined results for the two groups (a total of 49 experiences with "hygienic" treatment) were: 16 cured, 4 nearly cured, 13 improved, 12 stationary and 4 worse. Here, again, an excellent showing was made. Both for Cresatin and for the boric acid powder, the consistently favorable comment of the patients confirmed the results arrived at on paper. There were no untoward reactions.

Ointment of Benzoic and Salicylic Acid N. F.: Sixteen patients were tested in the "original" group. Four were cured, 2 nearly cured, 8 improved, 1 stationary and 1 worse. In the "supplementary" group, 9 in all, 1 was cured, none nearly cured, 3 improved, 3 stationary and 2 worse. The combined results for the two groups (25 experiences) were: 5 cured, 2 nearly cured, 11 improved, 4 stationary and 3 worse. In general, this ointment was useful in the earlier stages of our particular series of winter infections, but it stopped short of achieving cure. There were no untoward reactions.

Iodolate: Twenty-one patients were tested. The showing was fairly creditable in respect to therapeutic improvement; 3 cured, 1 nearly cured, 8 improved, 3 stationary and 6 worse. However, the percentage figure (28.5) of "worse" patients, which is bad enough, was accentuated by the severity of the untoward reactions, which were suppurative. In 3 patients a chemical dermatitis promptly developed. Moreover, a positive reaction resulted from patch tests employed on 2 of the "worse" patients. Accordingly, it was not tested further than in the original group of 21 patients, and a "supplementary" set of tests does not therefore appear in the table. Judged by our experiences, the preparation requires close medical supervision, and, moreover, is not equal therapeutically to certain other forms of treatment that we employed.

Pomeio: Eighteen patients were included in the group. Two were cured, none nearly cured, 6 improved, 2 stationary and 8 worse. In short, this preparation was decidedly inferior in our hands. Untoward

reactions were practically nil; at most, 3 patients exhibited superficial maceration which may have been referable to the alkaline nature of the preparation. They did not report any subjective symptoms.

Zephiran Chloride: Eighteen patients were employed. It became clear at the first examination (at the end of three weeks) that it was inferior to cresatin and "hygienic" treatment, and later it was found to be inferior in general under the circumstances of our tests. Eventually 1 patient was cured, 1 was nearly cured and 4 were improved; 8 were stationary, and 4 were worse. Moreover, the results were no better at the end of six weeks. There were no untoward reactions.

Results of Tests (117 Patients, 200 Experiences)

	Cresatin	Hygienic	Benzoic-Salicylic Acid Ointment	Iodolate	Pomeio	Zephiran	Totals
Patients in original group.....	24	20	16	21	18	18	
Cured (A)							
Original tests....	9	6	4	3	2	1	25
Supplementary...	7	10	1	0	0	0	18
Total experiences	16-23.1%	16-32.7%	5-20%	3-14.2%	2-11%	1-5.5%	43-21.5%
Nearly cured (B)							
Original tests....	1	3	2	1	0	1	8
Supplementary...	6	1	0	0	0	0	7
Total experiences	7-10.1%	4-8.1%	2-8%	1-4.7%	0-0	1-5.5%	15-7.5%
Improved (C)							
Original tests....	7	1	8	8	6	4	34
Supplementary...	21	12	3	0	0	0	36
Total experiences	28-40.5%	13-26.5%	11-44%	8-38.1%	6-33.3%	4-22.2%	70-35%
Stationary (D)							
Original tests....	7	7	1	3	2	8	28
Supplementary...	9	5	3	0	0	0	17
Total experiences	16-23.1%	12-24.4%	4-16%	3-14.2%	2-11%	8-44.4%	45-22.5%
Worse (E)							
Original tests....	0	3	1	6	8	4	22
Supplementary...	2	1	2	0	0	0	5
Total experiences	2-2.9%	4-8.1%	3-12%	6-28.5%	8-44.4%	4-22.2%	27-13.5%
Total experiences..	69	49	25	21	18	18	200
Totals of favorable results							
A + B =.....	33.2%	40.8%	28%	18.9%	11%	11%	
A + B + C =....	73.7%	77.3%	72%	57%	44.3%	33.2%	

COMMENT ON MEDICAMENTS

As shown by the totals at the bottom of the table, and considering the results for only the "cured" (*A*) and "nearly cured" (*B*) patients because they are the most unequivocal, Cresatin and "hygienic" (boric acid powder) treatments stand far ahead of the others. When the results for "improved" patients (*C* in the table) are added to these ($A + B + C$), ointment of benzoic and salicylic acid N. F. enters the picture. Now the results are singularly uniform—73.7 per cent for Cresatin, 77.3 per cent for boric acid and 72 per cent for the ointment. In other words, all of these 3 forms of treatment resulted in improve-

ment (or better) in about three quarters of the cases. It also shows that ointment of benzoic and salicylic acid shifts the results in our table toward improvement but does not make a good showing in respect to cure. By way of supplementing this evaluation, the table may be studied from the reverse direction—namely, of poor ("worse") results. Now it is noted that less than 3 per cent of the patients became worse under treatment with Cresatin, thus decidedly strengthening its showing.

It is clear from the table that Cresatin and hygienic treatments made the best showings and were nearly equal in value. However, there are several considerations which cannot appear in the table because we could not reduce them to statistics but which must be given weight in a final evaluation. We refer to the promptness in the therapeutic response to Cresatin, the absence of untoward reactions and the personal satisfaction of patients with this medicament. In short, considering all factors in the situation—statistical, clinical impressions and patients' opinions—we feel that there is a certain balance of evidence in favor of Cresatin over the boric acid powder.

Hygienic (boric acid powder) treatment, besides producing favorable results in our patients, raised the question of the preference for powders over other forms of agents, particularly in view of their associated drying powers and convenience of applications. This led to a second series of tests, at another penitentiary, wherein Cresatin was exhibited in powder as well as in liquid form. The results will be reported fully elsewhere. Suffice it to record here that results were disappointing. Incidentally, in this second set of tests, Cresatin (liquid) was found superior to the hygienic treatment, which was again tested for control purposes.

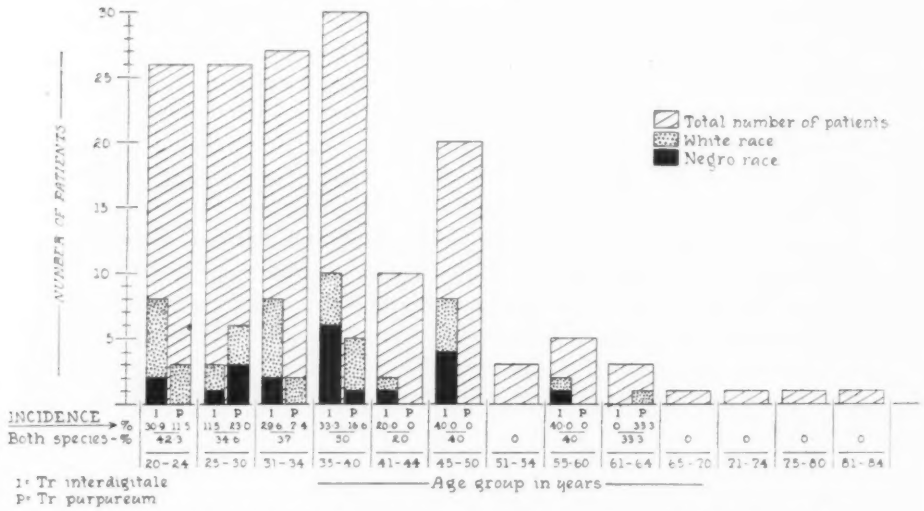
Confirming our previous clinical impressions, ointment of benzoic and salicylic acid tended to result in improvement only up to a certain point; i. e., short of the disappearance of hyperkeratosis. This was the case at both of the penitentiaries.

SUPPLEMENTARY OBSERVATIONS

In addition to the foregoing evaluation of medicaments, our data supplied information concerning certain other aspects of intertriginous infection. Some required such extensive reports that they will appear in separate, subsequent communications, but the ones requiring less extensive discussion will be recorded forthwith. We have analyzed our records in several directions, but only those findings that appear to have significance will be recorded. Once again, they should be regarded only in the light of winter infections. The basis for computations in the several phases of the data (age, race, species of culture, etc.) will be found to vary because we took advantage of the larger

figures that were available in some circumstances than in others. Thus, where the factor of treatment entered the picture, we were confined to the data on 117 cases, but the data were larger when only race, age and cultures were concerned, because we were able to include some of the patients who did not persist in the treatment prescribed and were dropped.

Age.—The average age of 154 patients was 35 years. The youngest was 20 years old. Only 10 per cent were older than 50. Prior to age 50, the several age groups were evenly distributed; that is, there was not any preponderance of patients around age 25, age 30, etc., with the exception of one group. Thus, there was a striking scarcity of cases from age 41 to 44 which we cannot explain. After age 50, there was a striking decrease in incidence.



Species of fungi in relation to age and race, occurrence of 58 cultures from 154 patients. (The 1 culture of Epidermophyton inguinale that was secured is not represented in this chart; this fact will account for an apparent discrepancy between the percentages in the chart and certain ones in the text.)

As to cultures, prior to age 41, growth was secured from 42 per cent of the patients; after age 41, from 20 per cent. T. purpureum infections fell preponderantly in the years prior to middle life (16 of the 17 cases). After age 40, there was only 1 example of T. purpureum infection but there were 12 examples of T. interdigitale infection. The ratio of infections due to T. purpureum to those due to T. interdigitale was 1:2 prior to age 41 but only 1:12 after age 40. That is, prior to age 41, T. purpureum infections were found to occur about six times as frequently as T. interdigitale infections. To sum up, whereas T. interdigitale remains the most frequent species when considered for

all ages, the earlier years appeared to predispose to T. purpureum infection in our patients.

As to severity of lesions, our data were significant as to age only in that severe infections occurred more frequently in age group 35 to 50, middle life. For this we have no explanation.

Race.—Race had a clearcut relationship to the mycology in the case. As to frequence of culture, a total of 154 patients, both Negro and white, yielded 59 positive cultures (38.3 per cent). Twenty-one of 41 Negro patients gave positive cultures (51.2 per cent), and 38 of the 113 white patients yielded positive cultures (33.6 per cent). This ratio of 51:33 has significance. Among the Negroes, T. interdigitale occurred seventeen times and T. purpureum only four. This gives a ratio of approximately 4:1 among them, whereas the ratio in the white patients was 2:1, as may be seen from the chart. In other words, T. purpureum was encountered twice as frequently in white patients.

As to types of lesions, only two appeared to have significance in respect to race. The hyperkeratotic one ("soft corn") occurred sixfold more frequently in the Negro race. Plantar vesicles were three times more common in Negroes.

Type of Lesion.—Scaliness was observed in the large proportion of cases that might be expected. Maceration appeared in about half of the cases, whether the lesions were simply scaly or were hyperkeratotic. Newly developed plantar vesicles appeared in about 16 per cent of the patients; the remains of vesicles in 6 per cent. Hyperkeratotic lesions were represented between the toes in 24 per cent. The "purpureum" type of dermatophytosis recently identified by Lewis[5] was represented clinically in about 7 per cent of the patients—on the ankles, instep and soles. Only 3 cases of frankly eczematoid dermatoses were included in our experience.

These different types of lesions have been analyzed in respect to (1) species of fungus concerned, (2) race and (3) effectiveness of treatment, with results as follows:

As to the fungi in the case, from macerated lesions cultures were secured in 44.4 per cent of the attempts, as against 37.9 per cent for lesions as a whole; the proportion of T. interdigitale to T. purpureum was the same as for lesions as a whole.

For hyperkeratotic lesions (without maceration), the statistics pointed the same way as for macerated lesions, but even more emphatically in one respect. Thus, cultures were secured in a larger number of attempts (57.1 per cent); the ratio of T. interdigitale to T. purpureum remained the same as for lesions as a whole.

5. Lewis, G. M.; Montgomery, R. M., and Hopper, M. E.: Cutaneous Manifestations of Trichophyton Purpureum (Bang), Arch. Dermat. & Syph. **37**:823 (May) 1938.

From vesicular lesions, cultures were secured in the same ratio of frequency as for the entire series of lesion types, but there was a great preponderance of T. interdigitale; the ratio was 5:1, as against the expected ratio of about 2:1 when based on all classes of lesions. In short, T. interdigitale occurred 2.5 times as frequently in vesicular lesions as in lesions in general. This tends to support Lewis'[5] thesis that T. interdigitale induces an acute type of infection.

As to the relationship of race to particular types of lesions, hyperkeratosis occurred seven times more frequently in Negro patients. Maceration occurred nearly twice as frequently in the Negroes; plantar vesicles three times as frequently. We did not analyze scaliness in detail, because it is common to nearly all lesions; nor fissuring, because it varies so rapidly in the same patient. The number of patients with lesions of "purpureum type" (see Lewis[5]) was so small (only 9) that it was inadequate for analysis.

As to the selectivity of one particular form of treatment for a particular type of lesion, conclusions are not permissible because so many medicaments were tested (6) that the results of analysis could not be significant; obviously, only a few of each type of lesions would receive a given form of treatment. However, some information was secured that was at least suggestive when the analysis was based on several forms of treatment. Incidentally, results of treatment were here evaluated on the basis of both "cured" and "almost cured" infections, on the one hand, and on "worse" infections on the other; infections that were simply "improved" were not included because they are so equivocal. In the foregoing circumstances, hyperkeratotic lesions were twice as refractory to treatment. Macerated lesions responded pari passu with lesions as a whole, but there were few indeed that became worse at any time. In fact, a large bulk of "improved" lesions makes it appear that macerated lesions responded in general more favorably than the average. Plantar vesicles responded best; 41 per cent were cured or almost cured, against an average of 28 per cent for all cases. In short, vesicular and macerated lesions cleared the most satisfactorily, while hyperkeratotic ones were the most resistant.

Comparison of T. Interdigitale and T. Purpureum in Relationship to Types of Lesions Produced and Cure.—Lewis[5] has asserted that a distinctive type of dermatitis is induced by T. purpureum and that it is more resistant to treatment than that produced by other organisms. We regret that we cannot confirm his thesis in its entirety, because it would mean a long step in advance in the prognosis and treatment of dermatophytosis. At the same time, we cannot quite dispute one part of it, namely that T. purpureum produces a distinctive type of lesion, because we realize that we have not acquired the proficiency

that he has in these premises and did not have so large a number of cases for study. In any event, of nine diffuse and subacute lesions involving the ankles, which we interpreted as of Lewis' T. purpureum type, we isolated T. interdigitale from 3 and T. purpureum from 1; the other 5 were negative for fungi. Moreover, T. purpureum occurred in severe infections (meaning extensive or acute) twice as often as T. interdigitale.

However, we can speak definitely in the matter of treatment because the personal equation is not involved in the identification of cultures or the recognition of cure. Unlike Lewis, we found that 50 per cent of the infections caused by T. purpureum were cured, contrasted with 32.4 per cent of those due to T. interdigitale. To sum up, the findings of Lewis were not confirmed in this penitentiary, particularly as to the resistance of T. purpureum to treatment. Perhaps the factor of winter dermatophytosis accounts for part of this discrepancy.

SUMMARY AND CONCLUSIONS

Under the excellent control and uniformity of conditions of a penitentiary, 117 inmates having winter dermatophytosis were selected as test objects for six different forms of treatment. Of these, metacresylacetate (Cresatin) is regarded by us as superior, but a simple boric acid powder was almost as efficient.

Response to treatment was poorest in hyperkeratotic lesions and best in vesicular and macerated ones.

Lesions caused by T. purpureum were not particularly distinctive and were not more resistant to treatment than other lesions.

Negroes were far more liable to hyperkeratotic and to macerated lesions and to plantar vesicles.

A remarkably high percentage (37.9) of positive cultures was secured, although only one attempt was made for each patient. They were obtained twice as frequently prior to age 41, were obtained far more frequently from Negroes (51:33) and were secured from 57 per cent of the hyperkeratotic lesions. T. interdigitale was, as usual, by far the commonest species. Infections due to T. purpureum were confined, almost entirely, to years prior to middle life and occurred twice as frequently in the white race. Epidermophyton inguinale was isolated only once. The type of lesion appeared to influence the percentage of positive cultures secured; both hyperkeratotic and macerated lesions were outstanding. They yielded 50 per cent and 100 per cent more positive cultures than the average. We submit these data in respect to cultures in the sense only that they indicate the circumstances at a particular penitentiary. They cannot be representative for dermatophytosis at large.

PENICILLIN OINTMENT IN THE TREATMENT OF SOME INFECTIONS OF THE SKIN

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MANY reports from English and American investigators indicate that local applications of penicillin are useful in the treatment of pyogenic infections of the skin. Bodenham [1] found that a penicillin cream was effective in eliminating streptococci and staphylococci from burns and surface wounds. Roxburgh, Christie and Roxburgh [2] prepared a penicillin ointment and a penicillin spray. They reported that local applications of penicillin were effective in the treatment of sycosis barbae and impetigo. Taylor and Hughes [3] applied penicillin ointment and penicillin in a spray to lesions of impetigo, sycosis barbae and furunculosis, with favorable results. Sophian and Connolly [4] treated acute and chronic pyogenic infections of the skin with a penicillin ointment containing a wetting agent. The results were good, especially in furunculosis and sycosis barbae. Schoch [5] applied the washings of "empty" penicillin ampules to the lesions of 4 patients with diseases of the skin and was enthusiastic as to the results. Johnson [6] prepared an ointment contain-

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Studies, observations and reports from the dermatologic departments of the Barnard Free Skin and Cancer Hospital and Washington University School of Medicine (Service of Dr. M. F. Engman Sr.).

1. Bodenham, D. C.: Infected Burns and Surface Wounds: The Value of Penicillin, Lancet **2**:725 (Dec. 11) 1943.

2. Roxburgh, I. A.; Christie, R. V., and Roxburgh, A. C.: Penicillin in Treatment of Certain Diseases of the Skin, Brit. M. J. **1**:524 (April 15) 1944.

3. Taylor, P. H., and Hughes, K. E. A.: Infective Dermatoses Treated with Penicillin, Lancet **2**:780 (Dec. 16) 1944.

4. Sophian, L. H., and Connolly, V. J.: The Use of Penicillin in Topical Application, Am. J. M. Sc. **208**:577 (Nov.) 1944.

5. Schoch, A. G.: Local Penicillin Therapy, Arch. Dermat. & Syph. **50**:202 (Sept.) 1944.

6. Johnson, H. M.: Penicillin Ointment for Pyodermas, Arch. Dermat. & Syph. **51**:270 (April) 1945.

ing penicillin and found that it was effective in the treatment of certain pyogenic infections of the skin. Templeton, Clifton and Seeberg [7] found that penicillium gauze, solutions of crude penicillin and purified penicillin in ointment bases were valuable therapeutic agents in the treatment of pyogenic infections of the skin. Cohen and Pfaff,[8] using penicillin by injection and penicillin ointment, obtained satisfactory results in 100 cases of pyogenic infections, including impetigo, sycosis barbae and "so-called" tropical ulcer. Wrong [9] treated 93 patients with cutaneous infections with a penicillin ointment and also reported excellent results in impetigo and sycosis barbae, although relapses were frequent in cases of sycosis barbae.

We treated 48 patients with pyogenic infections of the skin with penicillin ointment. The ointment was made with sterile materials under aseptic conditions. The ointment base was water miscible and contained glyceryl monostearate, stearic acid (U.S.P.), Duponol, a preservative (propyl ester of parahydroxybenzoic acid in a concentration of 0.08 per cent) refined peanut oil and distilled water. The peanut oil was added to prevent caking and drying on application. The p_H of this ointment was approximately 6.5. Penicillin sodium (commercial, Chas. Pfizer & Company, Inc., Brooklyn) which had been pretested by the United States Food and Drug Administration was added to the base in a concentration of 500 Oxford units per gram. When tested by the Standard Food and Drug Administration method for antiseptic ointments, this penicillin ointment gave a zone of penetration of 16 mm. with Staphylococcus aureus. The penicillin sodium contained in the ointment was stable to a high degree for a period of at least six months at refrigerator temperature (below 10 C.).

Before treatment was begun cultures were obtained from almost all the patients. The patients were directed to keep the ointment in a refrigerator when not in use. At first, directions were given to apply the ointment seven to eight times a day. Later, a few patients were directed to apply the ointment four times a day. The results appeared to be about the same in both groups, so that most of the patients were told to apply the ointment four times a day.

DISEASES TREATED

Impetigo.—Twenty-one patients with impetigo were treated by local applications of the penicillin ointment. Staph. aureus was found

7. Templeton, H. J.; Clifton, C. E., and Seeberg, V. P.: Local Application of Penicillin for Pyogenic Dermatoses, Arch. Dermat. & Syph. **51**:205 (March) 1945.

8. Cohen, T. M., and Pfaff, R. O.: Penicillin in Dermatologic Therapy, Arch. Dermat. & Syph. **51**:172 (March) 1945.

9. Wrong, N. M.: Penicillin Therapy in Skin Infections, Canad. M. A. J. **52**:341 (April) 1945.

on culture from all but 3 of these patients. The reports on cultures for these 3 were: Staphylococcus albus, diphtheroids and no growth, respectively. The most favorable results were obtained in this group of patients. Thirteen patients were cured. The average length of time to complete the cure was 5.8 days. Six patients were decidedly improved in an average of 7.5 days. Many of these patients did not return for follow-up visits. In 2 of the patients a contact dermatitis developed during treatment. This was noted five days after treatment was begun in 1 case and fourteen days after treatment was begun in the other. This will be discussed in detail later.

Secondary Infections.—A group of 17 patients with secondary infections of the skin were treated with the penicillin ointment. The eruptions might be classified as pyodermas. Included were 4 patients with acne vulgaris with large pustules of the face, 3 with nummular eczema in which the eczematous lesions were studded with pustules and 2 with pemphigus with pustular lesions on the body; others had infections following burns, and 1 had herpes simplex of the face. Staph. aureus was found on culture in 10 cases; Staph. albus, in 6 cases, and a contaminant, in 1 case. The secondary infection responded to treatment with the ointment, although the length of time necessary to produce improvement was much longer than for impetigo. The average duration of treatment was 22.5 days. In 1 case treatment was classified as a failure, and in 1 case contact dermatitis was noted seven days after treatment was begun.

In most of the cases treatment was instituted for the original disease after the infection improved.

Sycosis Vulgaris.—Five patients with sycosis vulgaris were treated. Cultures were reported as yielding the following organisms: Staphylococcus albus (2); Staph. aureus (1); diphtheroids (1), and no growth (1). Three of the patients responded favorably. In 1 of these persons the eruption tended to recur. Two relapses were treated in this patient with favorable results. Two patients responded to treatment, but a contact dermatitis developed in three days in one and in fifteen days in the other following the beginning of treatment.

Miscellaneous Infections of the Skin.—After thirty-six days of treatment, 1 patient with furunculosis was improved. One patient with a recurrent pustular eruption of the hands and feet was not improved after seventeen days of treatment. A patient with an infection of the hand and lymphangitis of the arm was improved after the hand had been treated for two days with hot soaks followed by the ointment. This patient did not return for observation after the second visit. A white woman, for whom a diagnosis of pyoderma faciale[10] was made, was

10. O'Leary, P. A., and Kierland, R. R.: Pyoderma Faciale, Arch. Dermat. & Syph. **41**:451 (March) 1940.

treated and cured in twenty-eight days.[11] A patient with a staphylococcic dermatitis was improved in seven days.

REACTIONS TO TREATMENT

Contact dermatitis developed in 5 of the 48 patients (10.4 per cent) while they were being treated with the penicillin ointment. The contact dermatitis was characterized by erythema, edema and vesicles in some of the patients. The dermatitis appeared in from three to fifteen days after the beginning of the treatment and cleared promptly when treatment was stopped. Two of the cases are reported in detail.

REPORT OF CASES

CASE 1.—L. A., a 52 year old white man, on Feb. 12, 1945 complained of an eruption about the nose of three days' duration. This followed an attack of influenza. Examination revealed a vesicular and pustular eruption on the upper lips and cheeks about the nose. The diagnosis was secondary infection of herpes simplex. A culture of the lesions revealed Staph. albus. He was given the ointment and instructed to apply it five or six times a day.

On February 13 there was much improvement in the pustular lesions.

On February 19 an erythematous and vesicular eruption was noted which involved the lower two thirds of the face and the eyelids. Use of penicillin ointment was discontinued, and the patient was instructed to apply cold towels every hour.

On February 22 there was some improvement in the dermatitis of the face.

On February 24 the dermatitis was nearly well.

CASE 2.—J. F., a 53 year old white woman, on May 26, 1945 complained of an eruption of the face of about four days' duration. Examination revealed a typical impetigo involving the sides of the face and the chin. The organism cultured was Staph. aureus. She was given the penicillin salve to apply four times a day.

On May 28 the old lesions were improved, but there were a few new lesions.

On May 31 the patient complained of severe itching of two days' duration. Examination revealed an erythematous and scaling eruption of the sides of the face with some swelling of the face. The impetigo was improved. The use of penicillin ointment was discontinued, and the patient was instructed to apply cold towels.

On June 1 the dermatitis was much improved.

On June 4 the dermatitis had completely disappeared. Two small areas of impetigo remained.

The impetigo cleared in a few days after application of ammoniated mercury ointment.

PATCH TESTS

Of the patients in whom contact dermatitis developed during treatment, 2 were available for patch tests. The patch tests were performed in the following manner.

Three samples of commercial penicillin sodium dissolved in isotonic solution of sodium chloride (10,000 units per cubic centimeter) were applied to gauze and

11. This patient was observed six months later and had not had any relapse.

placed on the skin. Saline solution was used as a control and applied in the same manner. The ointment base and peanut oil (as used in the ointment) were applied to patches of gauze and placed on the skin.

Positive reactions to all the patches with penicillin were observed, with erythema and edema in 1 patient and vesicles in the other. Negative reactions were observed to the saline solution, the peanut oil and the ointment base. In 1 of the patients a flare-up at the site of the previous contact dermatitis was observed after the patches had been applied.

COMMENT

The penicillin ointment which we used in our clinical trials was developed after extensive studies of ointments. It was chosen because of the stability of the penicillin in the ointment and because the release of penicillin from this type of ointment was found to be greater than from other types of ointments. Our clinical studies have shown that penicillin in this ointment is effective in the treatment of certain staphylococcic infections of the skin. The best results were obtained in the treatment of impetigo. Almost all the patients with this disease were cured. Decided improvement was noted after its use against furunculosis. One of the patients treated for sycosis vulgaris had several relapses, but each relapse was adequately controlled with the ointment. Secondary cutaneous infections accompanying certain other diseases of the skin were treated and were for the most part improved. No studies were done to determine whether or not the organisms involved became resistant to penicillin.

Patch tests on 2 of the patients in whom contact dermatitis developed during treatment gave us valuable information as to the antigenic agent of the contact dermatitis. These 2 patients were found to be extremely sensitive to patch tests with three separate batches of the penicillin sodium (dissolved in isotonic solution of sodium chloride). Other investigators who used penicillin locally have reported contact dermatitis in certain patients. Patch tests have been used by some of them. Cohen and Pfaff found that 5 patients of their series were sensitive to penicillin, 4 of them presenting an acute reaction to the drug after application. They performed patch tests with the ointment and found that 0.95 per cent of 524 subjects reacted to it. Wrong made patch tests with a "penicillin emulsion" and found that positive reactions developed in 2 patients who had had a dermatitis after local application of this "penicillin emulsion". The "emulsion" itself was used as a control, with negative results. We know that contact dermatitis can develop in people who handle penicillin and its salts. Pyle and Rattner [12] reported the first case and

12. Pyle, H. D., and Rattner, H.: Contact Dermatitis from Penicillin, J. A. M. A. **125**:903 (July 29) 1944.

observed positive reactions to penicillin patch tests with itself. Silvers [13] performed patch tests on a chemist who had acquired a dermatitis while handling amorphous penicillin and observed a positive result.

Our clinical impressions after we have used penicillin ointment for several months are these: While impetigo cleared up with penicillin ointment the results are no better than when ammoniated mercury or bismuth tribromphenate (xeroform) are used. Sycosis vulgaris is definitely improved in some cases when penicillin ointment is used, but the results do not appear to be any better than those obtained with the use of compound ointment of oxyquinoline sulfate. From the limited studies thus far made, in treatment of secondary infections penicillin ointment does not appear to produce any better results than the older antiseptics. Since the percentage of reactions to penicillin salve is relatively high and some of the reactions are rather severe, we feel that this drug may prove to be less useful in the treatment of cutaneous infections than some of the older antiseptics. The product seems to produce improvement somewhat faster than the older drugs, but this does not overcome the advantage of the older drugs from the standpoint of stability, availability and cost.

CONCLUSIONS

1. The penicillin ointment which was used in our clinical trials was effective in the treatment of certain pyogenic infections of the skin. It was most effective in the treatment of impetigo.

2. In 5 of the 48 patients (or 10.4 per cent) who were treated with the ointment contact dermatitis developed.

3. By means of patch tests, 2 of these patients were proved to be sensitive to penicillin sodium. In our opinion the other 3 were undoubtedly sensitive to penicillin sodium, but we were unable to prove this by patch tests.

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13. Silvers, S. H.: Contact Dermatitis from Amorphous Sodium Penicillin, Arch. Dermat. & Syph. **50**:328 (Nov.) 1944.

ACNE INDURATA IN IDENTICAL TWINS TREATED BY PENICILLIN

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THE *Quarterly Cumulative Index Medicus* contains references to many articles on diseases occurring simultaneously in identical twins. However, there are almost no articles concerning diseases of the skin in such persons, and none whatever concerning acne.

The literature contains a few articles dealing with the treatment of acne with penicillin.[1] In general, it has been found that the drug has been of little value against this disease, although it must be noted that the doses were relatively small and the treatment was continued for only a short time. With these facts in mind, it seems worth while to report the use of penicillin in treating a pair of identical twins for acne indurata with accompanying subcutaneous abscesses.

Jack and Gene H. were first seen by me in November 1944. There were seven other children in the family, one of whom, a younger girl, had mild acne. The twins were born in May 1927, and as children they suffered at the same time from chickenpox, whooping cough and measles. Their acne began in the same month of 1941. It is of interest that these boys had always been inseparable; they had even insisted on sleeping together.

The 2 boys had been under the charge of another dermatologist for practically two years. They had received the usual treatments for acne, with little improvement; roentgen and ultraviolet irradiation, diet, various lotions and plenty of vitamins had accomplished practically nothing.

Physical examination showed that the boys were of almost the same height and that each weighed 131¼ pounds (59.5 Kg.). Their muscular development was poor. Each had the usual pustular acne of face, neck, torso, arms and upper part of the thighs; in addition, there were scattered lesions of acne indurata, chiefly on the face and neck. Both showed subcutaneous abscesses, some of which had coalesced into lesions of as much as 4 inches (10 cm.) in diameter on the body and limbs. There was little acne on Jack's chest except at the edges of a practically solid mass of scar tissue.

Both boys were given the usual acne diet, solution of potassium arsenite U. S. P., wet dressings of magnesium sulfate, a solution of salicylic acid in alcohol and acetone, 5 per cent sulfathiazole in vanishing cream, ultraviolet radiation from a cold

1. Cohen, T. M., and Pfaff, R. O.: Penicillin in Dermatologic Therapy, Arch. Dermat. & Syph. **51**:172 (March) 1945. Franks, A. G.; Dobes, W. L., and Romano, D.: Penicillin in the Treatment of Cutaneous Disease, ibid. **52**:14 (July) 1945. Morginson, W. J.: The Clinical Use of Penicillin in Dermatology, South. M. J. **38**:320 (May) 1945.

quartz mercury vapor lamp, and the opening and draining of pustules and abscesses. In cultures from the abscesses of both boys was a heavy growth of Staphylococcus albus. By the middle of March both boys were slightly improved.

On March 25, through arrangement with Dr. C. J. Van Slyke, of the United States Public Health Service, I received a 20 cc. vial of penicillin in yellow wax U. S. P. and peanut oil. On March 26, I began to treat Gene with this preparation as an ambulatory patient; he received 100,000 units in the morning and 200,000 in the late afternoon. On April 3 my supply of this preparation had run out and no more was obtainable. The improvement had been so great that it was decided to continue treatment for four days more with 100,000 units in water three times a day.

On April 20 practically all abscesses had disappeared and there were only two or three lesions of indurated acne remaining, but about half of the superficial acne still remained on both the face and the back. Gene had gained weight; his appetite was much better, and there was a decided change in his mental attitude.

On April 9 Jack entered the Suburban Hospital, where he remained through April 19, receiving 50,000 units of penicillin every three hours, a total of 300,000 units a day. On April 20 it was noted that there was great improvement but that on the site of several of the old abscesses small granulomas had developed. He was given an ointment for these consisting of 100,000 units of penicillin in 1 ounce (30 Gm.) of hydrous wool fat and white petrolatum base, with directions to use it once a day after a bath. The result was gratifying, and by April 25 the granulomas had practically disappeared.

On September 17 both boys were seen. Each had gained weight; Gene weighed 134 pounds (60.8 Kg.), and Jack weighed 133¼ pounds (60.4 Kg.); neither had any deep abscesses or granulomas, but both showed one or two lesions of acne indurata on the face and neck and mild acne on the trunk. In addition, Jack had a few acne lesions on his forearms.

In conclusion, it may be said that these identical twins were cured of chronic subcutaneous abscesses associated with acne indurata; that the acne indurata had been greatly improved, and that the underlying acne had been somewhat helped. There was no essential difference in the results obtained with penicillin dissolved in yellow wax and peanut oil and those obtained with penicillin dissolved in water.

PENICILLIN IN TOPICAL TREATMENT OF PYOGENIC INFECTIONS OF THE SKIN

Clinical and Laboratory Observations

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THIS study was designed to correlate the clinical results of topical penicillin therapy for a group of superficial infections of the skin, with the sensitivity to penicillin in vitro of the organisms isolated. The widespread topical use of penicillin makes such a study desirable. Because penicillin is relatively nonirritating to the skin and nonsensitizing and because of its dramatically prompt action in favorable cases, the drug is admirably suited for the topical treatment of superficial pyogenic infections. Penicillin incorporated into ointment base is sufficiently stable if properly stored. Indeed, the rate of deterioration of the ointment is such that it may even be kept at room temperature for several weeks without serious reduction of activity.[1] Better knowledge of its stability permits extending the use of pencillin for topical application among patients whose access to refrigeration facilities is limited.

Our investigation was undertaken at the suggestion of the Air Surgeon's Office, Headquarters, Army Air Forces, to demonstrate why certain pyodermas respond promptly to application of the antibiotic and others do not. We present results in 45 cases of varied pyodermas studied clinically and bacteriologically at an Army Air Forces hospital in Florida. This is only a fraction of the patients with dermatologic diseases that we have treated with penicillin. The material is classified by diagnosis in tables 1, 2 and 3. On culture the majority of lesions yielded either beta hemolytic Streptococcus (Lancefield group A, C or G) or hemolytic Staphylococcus aureus, or both. Nonhemolytic Staph. aureus was isolated in 2 cases. Anaerobic as well as aerobic conditions of cultivation were utilized. All strains of staphylococci isolated were found to be positive for the presumptive pathogenicity tests of production of coagulase and fermentation of mannitol. In addition to the organisms

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1. Gots, J. S., and Glazer, A. M.: Stability and Activity of Penicillin in Solution and in Ointment, War Med. **7**:168 (March) 1945.

named, diphtheroids, Neisseria and other bacteria were cultivated. These were recognized as obvious bacteriologic vagrants and were not studied further.

PROCEDURE AND METHOD

The management of each case conformed to the following procedure: After the initial dermatologic examination the patient was referred to the laboratory for bacterial cultures. Treatment with penicillin ointment was then carried out, three or four times during the day, either in the hospital or on an outpatient status. No other drugs were used to supplement the applications of penicillin, and within forty-eight to seventy-two hours it was possible to appraise the results of therapy. We found that when no distinct improvement could be detected in three days none would probably be forthcoming with additional treatment. Excluding several persons with impetigo which healed rapidly, each patient was treated continuously for one to three weeks.

With few exceptions it was demonstrated that the staphylococci recovered from lesions resistant to treatment were resistant to penicillin from the start. Beta hemolytic streptococci literally undergo dissolution overnight after treatment with penicillin. These organisms do not as a rule assume characteristics of acquired resistance, and the eruptions which they produce usually clear up with amazing rapidity.

Penicillin sensitivity of the organisms was determined by a tube dilution turbidity method, employing the glucose–yeast extract broth described by Schmidt and Moyer.[2] The inoculum consisted of a twenty-four hour broth culture (2 to 8×10^8 organisms per cubic centimeter) diluted 1:100 in the broth medium. This served as the diluent for preparing the final penicillin concentrations of 5, 1, 0.5, 0.32, 0.16, 0.08, 0.05, 0.04, 0.02, 0.01 and 0.005 units per cubic centimeter. After twenty-four hours of incubation at 37 C., the tubes were examined for growth, macroscopic turbidity being used as the index. The end point recorded was that tube containing the least concentration of penicillin which completely inhibited the growth of the organisms. By this method, Staphylococcus aureus strain H (a standard sensitive strain used for assay purposes) was completely inhibited by 0.04 unit per cubic centimeter. Organisms which grew in 5 units per cubic centimeter were considered resistant. In cases in which these organisms were carried to higher concentrations, 100 to 500 units per cubic centimeter was still insufficient for inhibition.

Various concentrations of penicillin, from 166 units [3] to 1,600 units [4] or more per gram of base, have been prepared in ointments by different authors. The optimal concentration probably lies in the lower levels of this range. With Garrod,[5] we doubt that there is any great advantage in

2. Schmidt, W. H., and Moyer, A. J.: Penicillin: I. Methods of Assay, J. Bact. **47**:199 (Feb.) 1944.

3. Johnson, H. M.: Penicillin Ointment for Pyodermas, Arch. Dermat. & Syph. **51**:270 (April) 1945.

4. Cohen, T. M., and Pfaff, R. O.: Penicillin in Dermatologic Therapy: Report of Results in One Hundred Cases, Arch. Dermat. & Syph. **51**:172 (March) 1945.

5. Garrod, L. P.: Action of Penicillin on Bacteria, Brit. M. J. **1**:107 (Jan. 27) 1945.

highly concentrated preparations for routine use. The ointment we employed contained approximately 800 units of penicillin per gram. We have tried various ointment bases—emulsion-type base, petrolatum, petrolatum with hydrous wool fat, cholesterol-petrolatum mixture and petrolatum with liquid petrolatum—incorporating 100,000 units of the drug in 120 Gm. of the vehicle.[6] We are not convinced that one base is materially superior in therapeutic effectiveness to another with equivalent concentration of penicillin. However, mention must be made of the in vitro tests performed by Templeton and his associates,[7] which suggested increased penicillin activity with increased water content of the ointment. Our emulsion type base was abandoned after a few instances of contact dermatitis were encountered. At the present time we employ a base of simple petrolatum. Contact sensitivity to penicillin was not observed among the cases reported herein.

CLINICAL MATERIAL AND RESULTS

The group "infectious dermatitis" (table 1) was designated to include cases of true infectious eczematoid dermatitis (Engman), of secondarily infected eczematoid dermatoses (contact dermatitis, dermatophytosis or dermatophytid with predominating pyogenic features), of external otitis and of dermatitis repens. Significant is the demonstration of a high incidence of penicillin-resistant strains among the staphylococci isolated (six sensitive and seventeen resistant strains), and a correspondingly poor therapeutic response to topical applications of penicillin. The role of epiphenomena, such as allergic bacterial sensitization and "eczematization," to account for the resistance to therapy of many of these cases, cannot be analyzed because it was impossible at any time to eliminate the pathogenic bacteria from the diseased skin.

In contrast to the foregoing the cases of impetigo and ecthyma (table 2) exhibited a reversed incidence of penicillin resistance (10 sensitive, 2 resistant strains of staphylococci), and the results of treatment with penicillin were excellent in the majority of cases. Our experience in treating impetigo in many other cases, not included in this series, justifies enthusiasm for the effectiveness of locally applied penicillin. It will be observed that among the cases listed are 2 of infections with sensitive strains of staphylococci which failed to yield to treatment with penicillin. Ammoniated mercury ointment in 1 case and sulfathiazole ointment in the other produced prompt cures.

6. Since this study was made, we have reduced the concentration of penicillin to 300 units per gram of ointment, with no observable loss of efficacy.

7. Templeton, H. J.; Clifton, C. E., and Seeberg, V. P.: Local Application of Penicillin for Pyogenic Dermatoses, Arch. Dermat. & Syph. **51**:205 (March) 1945.

A reassay of sensitivity to penicillin, to determine if fastness may have supervened, was unfortunately not performed.

The group "folliculitis" (table 3) included cases of involvement of the beard, neck and legs. Staphylococci exclusively were isolated—

TABLE 1.—*Infectious Dermatitis: Summary of Bacteriologic and Therapeutic Results*

Case No.	Diagnosis	Location	Duration	Culture *	Penicillin Inhibition (Units/Cc.) Staph.	Strep.	Therapeutic Result †
1	Infectious eczematoid dermatitis	Left foot	7 yr.	HSA, BHS	>500	.....	P
2	Infectious eczematoid dermatitis	Feet, legs, hands	7 mo.	HSA, BHS	>5	0.005	P
3	Infectious eczematoid dermatitis	Right foot	2 wk.	HSA, BHS	0.5	0.005	P‡
4	Infectious eczematoid dermatitis	Toes	10 days	HSA, BHS	>5	0.005	P
5	Infectious eczematoid dermatitis	Left palm, right sole	2½ yr.	HSA, BHS	0.01	0.0025	G
6	Infectious eczematoid dermatitis	Toes	5 days	BHS	...	0.005	G
7	Infectious eczematoid dermatitis	Left leg	1 yr.	HSA	>5	.....	P
8	Infectious eczematoid dermatitis	Feet	10 mo.	HSA	>5	.....	P
9	Infectious eczematoid dermatitis	Left foot	2 mo.	HSA	>5	.....	P
10	Infectious eczematoid dermatitis	Feet	1 mo.	HSA, BHS	>5	.....	P
11	Infectious eczematoid dermatitis	Right axilla	5 days	HSA	>5	.....	P
12	Infectious eczematoid dermatitis	Left ankle	2 mo.	HSA, BHS	>5	.....	F
13	Infectious eczematoid dermatitis	Forearm, right hand	2 yr.	HSA	>5	.....	P
14	Infectious eczematoid dermatitis, folliculitis	Ears, feet, chin	18 mo.	NHSA	>5	.....	P
15	Dermatophytosis, pyoderma	Toes	1 wk.	HSA, BHS	>5	0.005	F
16	Dermatophytosis, pyoderma	Toes	3 wk.	BHS	...	0.005	G
17	Dermatophytosis, pyoderma	Right foot	6 mo.	HSA	5	.....	F
18	Dermatophytosis, pyoderma	Toes	1 mo.	HSA, BHS	>5	0.005	F
19	Dermatophytosis, pyoderma	Left foot	2½ yr.	HSA, BHS	>5	.....	P
20	Otitis externa	Ears	9 mo.	HSA	>5	.....	P
21	Otitis externa	Ears	2 yr.	NHSA	0.05	.....	G
22	Otitis externa	Ears	1 yr.	HSA	0.04	.....	G
23	Contact dermatitis, pyoderma	Scalp, face	5 days	HSA	5	.....	G
24	Dermatitis repens	Right heel	3 mo.	HSA, BHS	>500	0.005	P
25	Dermatitis repens	Hands	2 yr.	HSA, BHS	>5	0.01	P

* HSA = hemolytic Staphylococcus aureus; BHS = beta hemolytic streptococcus; NHSA = nonhemolytic Staph. aureus.

† G = good result, cure complete or nearly complete; F = fair result, partial improvement or relapse; P = poor result, treatment ineffective.

‡ Sensitivity to emulsion type ointment base.

sensitive to penicillin in 4 and resistant in 3. Results of treatment in these cases were only fair. Our experience with a variety of these dermatoses, especially of folliculitis (sycosis) barbae, indicates that although rapid healing often takes place there is a decided tendency

toward recurrence. Other authors have also encountered the problem of frequent reinfection.[8]

Patients with acne vulgaris were not treated. Bacteria isolated from abscesses and pustules in a number of cases of severe acne which we have observed usually consisted of nonpathogenic staphylococci or penicillin-resistant staphylococci. In general, penicillin therapy for acne

TABLE 2.—*Impetigo and Ecthyma: Summary of Bacteriologic and Therapeutic Results*

Case No.	Diagnosis	Location	Duration	Culture *	Penicillin Inhibition (Units/Cc.) Staph.	Penicillin Inhibition (Units/Cc.) Strep.	Therapeutic Result †
26	Impetigo	Face	4 days	HSA	0.04	.....	G
27	Impetigo	Knee, face	1 wk.	BHS	....	0.005	G
28	Impetigo	Face, trunk	2 wk.	HSA	0.05	.....	G
29	Impetigo	Face, penis	10 days	HSA, BHS	0.04	0.005	G
30	Impetigo	Face	1 wk.	HSA	0.05	.....	P
31	Impetigo	Face, trunk	3 wk.	HSA, BHS	>5	.....	P
32	Impetigo	Face	1 wk.	HSA	0.05	.....	G
33	Impetigo	Abdomen	5 days	HSA	0.04	.....	G
34	Impetigo	Scalp, face	2 wk.	HSA, BHS	0.04	.....	G
35	Ecthyma	Legs	18 mo.	HSA, BHS	>5	.....	P
36	Ecthyma	Feet	4 wk.	HSA, BHS	0.05	0.01	P
37	Ecthyma	Right leg	10 days	HSA	0.02	.....	G
38	Impetigo, folliculitis	Face	2 mo.	HSA	0.08	.....	G

* HSA = hemolytic Staphylococcus aureus; BHS = beta hemolytic streptococcus.

† G = good result, cure complete or nearly complete; F = fair result, partial improvement or relapse; P = poor result, treatment ineffective.

TABLE 3.—*Folliculitis: Summary of Bacteriologic and Therapeutic Results*

Case No.	Diagnosis	Location	Duration	Culture *	Penicillin Inhibition (Units/Cc.)	Therapeutic Result †
39	Folliculitis	Beard	2 wk.	HSA	0.04	G
40	Folliculitis	Beard, neck	20 mo.	HSA	0.02	G
41	Folliculitis	Beard	2 yr.	HSA	>5	P
42	Folliculitis	Legs, face	18 mo.	HSA	>5	P
43	Folliculitis	Beard	1 yr.	HSA	0.05	G
44	Folliculitis	Beard	11 wk.	HSA	>5	P
45	Acne necrotica	Scalp, forehead	6 yr.	HSA	0.04	F

* HSA = hemolytic Staphylococcus aureus.

† G = good result, cure complete or nearly complete; F = fair result, partial improvement or relapse; P = poor result, treatment ineffective.

is hardly logical. The unfavorable results observed by others [9] confirm this conclusion. On the other hand, staphylococci from furuncles are found usually to be sensitive to penicillin.

8. (*a*) Taylor, P. H., and Hughes, K. E. A.: Infective Dermatoses Treated with Penicillin, Lancet **2**:780 (Dec. 16) 1944. (*b*) Roxburgh, I. A.; Christie, R. V., and Roxburgh, A. C.: Penicillin in Treatment of Certain Diseases of the Skin, Brit. M. J. **1**:524 (April 15) 1944.

9. Garrod.[5] Roxburgh, Christie and Roxburgh.[5b]

COMMENT

Data concerning the use of penicillin for the treatment of cutaneous infections caused by staphylococci indicate that the antibiotic, while eminently satisfactory in many cases, is far from universally effective. This study of an unselected series of cases of pyogenic dermatoses with regard to the bacteriologic observations and the degree of sensitivity to penicillin of the isolated organisms, particularly the staphylococci, provides an explanation for the sometimes erratic results encountered in topical therapy with penicillin. Approximately half of the patients infected with staphylococci alone or in conjunction with streptococci harbored penicillin-resistant strains (in 22 of 42 cases). A few patients exhibited initial improvement with applications of penicillin ointment; then their dermatoses remained at a stationary level or relapsed, a circumstance undoubtedly due to elimination of the streptococcus moiety of a combined infection, leaving the penicillin-resistant staphylococcus unaffected. (So far not one instance of resistance or fastness to penicillin has been encountered among the strains of beta hemolytic streptococci isolated, and we regard determination of the sensitivity to penicillin of these streptococci as an unnecessary routine procedure.) Moreover, we observed that when the resistance of a strain of staphylococci was of such degree that growth was not inhibited by 5 units of penicillin per cubic centimeter in vitro the strain would not respond to treatment with penicillin ointment containing 800 units in each gram. Certainly an infection with an organism so resistant will never respond to intramuscular injections of penicillin, by which average maximum blood levels of about 0.6 unit per cubic centimeter are generally attained. For purposes of expediency, therefore, we consider it unnecessary to carry testing of sensitivity to penicillin beyond the concentration of 5 units per cubic centimeter. It will be observed in table 1 that in 2 of our cases staphylococci not inhibited by 500 units of penicillin per cubic centimeter were isolated, and probably there were many more strains of highly resistant staphylococci in this series. Resistance of staphylococci to as high as 10,000 units of penicillin per cubic centimeter has been recorded.[10]

The question may be asked, Is it advisable in cases of pyoderma in which local treatment with penicillin is contemplated to perform routinely sensitivity studies on the bacteria? This can be answered in the negative. With penicillin ointment now readily available and relatively inexpensive, a therapeutic test, as we have shown, will yield practically the same information qualitatively as the sensitivity test. We have accumulated evidence that treating pyodermas with penicillin ointment may in some

10. Keyes, J. E. L.: Penicillin in Ophthalmology, J. A. M. A. **126**:610 (Nov. 4) 1944.

cases increase the degree of resistance of staphylococci to penicillin, thereby accounting for infectious relapse and failure of treatment. Fortunately, this is not of common occurrence. Taylor and Hughes [8a] reported that after treatment with an ointment containing 200 units of penicillin per gram certain sensitive strains of staphylococci from cutaneous infections became fast. They attributed the accident to poor diffusibility of penicillin from the ointment base and to deterioration. The difficulty did not arise with ointment containing 400 units of penicillin per gram. On the other hand, among a series of cases of infected wounds and abscesses treated with penicillin intramuscularly or intravenously, Gallardo [11] found that 9.4 per cent of coagulase-positive strains of staphylococci acquired fastness to penicillin during the course of treatment, in addition to 12.9 per cent of naturally resistant strains among the pathogenic staphylococci. Observations made by Crawford and King [12] among a group of infections of the eyes and lid margins indicated that when bacteriologic relapse occurred the responsible organisms were no less sensitive to penicillin than were the original invaders.

The importance of bacteriologic examination of the skin in augmenting the understanding of the pyodermas deserves great emphasis. Cultural investigations, we suggest, are especially valuable in studying chronic, treatment-resistant eczematoid eruptions. Clinical judgment and laboratory tests must be called on to decide whether the bacteria isolated are primary pathogens or secondary invaders of an underlying dermatosis and what treatment might be most effective under the circumstances. Claims for the efficacy of penicillin in topical dermatologic therapy therefore require thoroughgoing bacteriologic support. Lacking this, discrepancies of experience in treating pyodermas can be expected. It is possible that there are local differences in incidence of strains of staphylococci in various parts of the world, just as there are of hemolytic streptococci. Areas in which carriers of Lancefield group A streptococci abound are likely to show also an increased incidence of streptococcic contamination of the skin.[13] In subtropical Florida, staphylococci are found more frequently in pyodermas than are streptococci, but the material reported by Roxburgh [8b] from England gives bacteriologic observations almost identical with those in our own cases. There are no clinical features that distinguish pyodermas caused by penicillin-sensitive strains from those caused by penicillin-resistant strains.

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11. Gallardo, E.: Sensitivity of Bacteria from Infected Wounds to Penicillin: II. Results in One Hundred and Twelve Cases, War Med. **7**:100 (Feb.) 1945.

12. Crawford, T., and King, E. F.: The Value of Penicillin in the Treatment of Superficial Infections of the Eyes and Lid Margins, Brit. J. Ophth. **28**:373 (Aug.) 1944.

13. Hare, R.: Haemolytic Streptococci in Normal People and Carriers, Lancet **1**:85 (Jan. 18) 1941.

An attempt to explain the predominance of penicillin-resistant staphylococci among the patients with infectious dermatitis (table 1) stimulates conjecture regarding the host-parasite relationships which determine the characteristics of an inflammatory reaction. Needless to say, none of the patients in this study had had previous treatment with penicillin, and thus any possibility of induced resistance (fastness) is precluded. Most of the infections were chronic and indolent, which suggested invasion by organisms of low grade virulence. When various pathogens are made resistant to penicillin, a great and apparently permanent decrease in virulence occurs.[14] Similar loss of virulence has been reported in organisms resistant to sulfonamide compounds.[15] Also the incidence of resistance to penicillin is higher among nonpathogenic strains of staphylococci than among pathogenic strains. The nature of the inflammatory response, then, is dependent on the virulence of the organism, which, in turn, is apparently associated with its resistance to penicillin.

When resistance to penicillin increases, there is a reduction of the rate of growth and of enzymic activities of the organism,[16] and when the growth of an organism is retarded the host-parasite balance will be disturbed. Hobby, Meyer and Chaffee[17] have shown that penicillin is effective only when active multiplication is taking place. When the rate of growth of staphylococci decreases, the organisms become less susceptible to the action of penicillin. If the enzymic activities are greatly reduced with increased resistance there is no a priori reason why other products elaborated during normal metabolism (hemotoxin, lethal toxin, dermonecrotic toxin, leukocidin, Duran-Reynals spreading factor) should not also be affected.

Our analysis of clinical statistics reveals some distinct limitations of penicillin in the treatment of many staphylococcic infections. A number of valuable antibacterial drugs are available for topical treatment of penicillin-resistant infections of the skin—mercurials, sulfonamide compounds and chlorahydroxyquinoline, to name some common ones. A limited experience which we have had with tyrothricin for dermatologic infections suggests that it too is an effective antibacterial

14. McKee, C. M., and Houck, C. L.: Induced Resistance to Penicillin of Cultures of Staphylococci, Pneumococci and Streptococci, Proc. Soc. Exper. Biol. & Med. **53**:33 (May) 1943.

15. Horsfall, F. L., Jr.: The Effect of Sulfonamides on Virulence of Pneumococci, J. Clin. Investigation **21**:647 (Sept.) 1942.

16. Abraham, E. P.; Chain, E.; Fletcher, C. M.; Florey, H. W.; Gardner, A. D.; Heatley, N. G., and Jennings, M. A: Further Observations on Penicillin, Lancet **2**:177 (Aug 16) 1941. McKee and Houck.[14]

17. Hobby, G. L.; Meyer, K., and Chaffee, E.: Observations on the Mechanism of the Action of Penicillin, Proc. Soc. Exper. Biol. & Med. **50**:281 (June) 1942.

agent, in some respects superior to penicillin. Undoubtedly, more and more potent antibiotics or combinations of antibiotics will in time be developed, to the enhancement of dermatologic therapy.

SUMMARY AND CONCLUSIONS

The results of local treatment with penicillin ointment of pyogenic dermatoses are summarized as follows: (1) impetigo and ecthyma, results good; (2) folliculitis, results fair; (3) infectious dermatitis (including infectious eczematoid dermatitis, infected eczematoid dermatoses, dermatitis repens and external otitis), results poor.

The variation in results of treatment is accounted for by differences among strains of infecting staphylococci, as manifested by wide ranges of sensitivity to penicillin in vitro. A predominance of penicillin-sensitive staphylococci are isolated from lesions of impetigo, as contrasted with a predominance of penicillin-resistant staphylococci from the eczematoid lesions of infectious dermatitides. Resistant strains of beta hemolytic streptococci have not been encountered. The therapeutic results with penicillin topically parallel closely the degree of sensitivity to penicillin of the micro-organisms as determined in vitro.

Technical Sergeant Joseph L. Sardinas, Medical Department, Army of the United States, assisted in the laboratory procedures and Technical Sergeant Richard H. Swaine, Medical Department, Army of the United States, prepared the ointments.

TOKELAU IN GUATEMALA

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GUATEMALA

THE FIRST description of tinea imbricata, or tokelau, dates from the year 1686 when William Dampier,[1] in a record of his voyages, referred to a scaling cutaneous disease encountered in the Philippines, Mindanao, the Marianas and Guam. It was subsequently observed in the islands of the Pacific by Entrecasteux (1780),[2] Alibert (1832),[3] Meerderwoort (1839),[4] Fox (1844) [5] and Turner (1869).[6] The disease was not known in the Tokelau Islands until 1869, when it was introduced from the Gilberts.

In 1874 Tilbury Fox [7] demonstrated fungi in the squames, and the observation was confirmed in 1878 by Königer.[8] Manson (1879) [9] differentiated tokelau from herpes circinatus. Sabouraud [10] asserted that it was caused by Trichophyton. Many of the early attempts to culture the fungus failed, however, and led to the erroneous conclusion that it was a species of Aspergillus.

Tokelau was probably introduced into America in pre-Columbian times by immigrants from the Orient. Paranhos and Leme [11] observed a case in Brazil in 1904 and Mora Mora [12] reported a case (without

From the Universidad de San Carlos de Guatemala.

1. Dampier, W.: Voyage autour du monde, Paris, 1789.

2. Entrecasteux, cited by Manson.[9]

3. Alibert, J. L. M. A.: Précis théorique et pratique sur les maladies de la peau, ed. 2, Paris, Caille et Ravier, 1832.

4. Meerderwoort, cited by Manson.[9]

5. Fox, J. L.: Narrative of the United States Exploring Expedition, During the Years 1839, 1840, 1841, 1842 by Charles Wilkes, Philadelphia, Lea & Blanchard, 1845, vol. 5, pp. 40-41 and 104-105.

6. Turner, G. A.: Notes of Practice in Samoa, Glasgow M. J. **2**:502 (Aug.) 1870.

7. Fox, T.: On Tokelau Ringworm and Its Fungus, Practitioner **2**:304, 1874.

8. Königer: Ueber den polynesischen Ringwurm auf den Carolinen-, Gilbert- und Samoa-Inseln, Virchows Arch. f. path. Anat. **72**:403, 1878.

9. Manson, P.: Notes on Tinea Imbricata, an Undescribed Species of Body Ringworm, China Imp. Customs M. Rep. (1878) **16**:1, 1879; M. Times & Gaz. **2**:342, 1879.

10. Sabouraud, cited by Figueroa and Conant.[14]

11. Paranhos, U.: Tinea Imbricata in Brazil, J. Trop. Med. **7**:153, 1904. Paranhos, U., and Leme, C. P.: Note on the Tinea Imbricata in Brazil, ibid. **9**:129, 1906. Leme, C. P.: Contribuição ao estudo do tokelau, Rio de Janeiro, 1903.

12. Mora Mora, cited by Figueroa and Conant.[14]

mycologic study) in Colombia in 1935. Two cases were reported in El Salvador in 1937 and 1938. In Guatemala Dr. Francisco Diaz A.,[13] in 1937, presented a case before the Primer Congreso Sanatario Centro-Americano. That patient was examined in connection with the present study. A second Guatemalan case, with mycologic study, was reported by Figueroa and Conant.[14] Dr. Diaz, in a sanitary survey of Guatemala, has observed this mycosis in the states of Sololá, Chimaltenango, Suchitepequez and Huehuetenango.

The disease is known under many different names, among which are: tinea imbricata, pita, buckwar, oune, Kune-Kune, tukune-kune, gune, gogo, gugo, gugomon, cascado gorap, koerab, korab-besi, loesoeng, lusung, lofa-tokelau, etemane, talofat, kilinai, dermatosis chronica figurativa exfoliativa of Thomson, herpes desquamans of Turner, dermatomycosis koerab, tropical ichthyosis, herpes of Manson, sarna de Dajak and (in Guatemala) jiote.

The fungus, Trichophyton concentricum R. Blanchard 1895, also has a number of synonyms: Lepidophyton concentricum, Aspergillus lepidophyton, Aspergillus tokelau, Endodermophyton concentricum, E. indicum and E. tropicalis.

Tokelau is a contagious, inoculable, pruriginous, erythematosquamous dermatophytosis in which the scales form an annular concentric pattern which becomes modified by the confluence of the spreading rings. The infection is chronic (duration of sixty-four years in one of the cases in this series), it may involve the entire cutaneous surface, and it is resistant to treatment.

Lesions may develop from ten to twelve days after inoculation with infected scales and from fifteen to eighteen days after inoculation with a pure culture. They begin as small round vesicles which are replaced by reddish macules. The fungus penetrates the epidermis to the malpighian layer, where it grows readily, separating the stratum granulosum from the stratum corneum. Separation of these layers produces the characteristic scale, and peripheral growth of the lesion and repetition of the process in the older portions of the lesion result in the peculiar pattern of this dermatophytosis. There is pruritus, which is increased by certain foods, heat, salt water and exposure to the sun. Although any cutaneous surface may be involved, in the cases included in this series lesions were most prominent on the trunk.

The scale which is characteristic of tokelau is at first small, thin, dirty white or yellowish white. As it becomes thicker and larger it

13. Diaz A., F., in Primer congreso santario de Centro America y Panama, Guatemala, Impreso en la Typografia Nacional, 1937.

14. Figueroa, H., and Conant, N. F.: First Case of Tinea Imbricata Caused by Trichophyton Concentricum Blanchard 1896, Reported from Guatemala, Am. J. Trop. Med. **20**:287, 1940.

retains the same color. The most striking characteristic of this mycosis is the regular pattern of concentric arcs of circles. This pattern is formed by the scales, which become detached at the inner edge while the outer edge remains attached. As the diameter of the ring of scales increases by peripheral growth new rings form successively within the first, often at such frequent intervals that the scales of the outer ring may overlap those of the second as the tiles on a roof. Each successive ring can be felt as a ridge if a finger is rubbed radially across the lesion. Autoinoculation by scratching initiates new lesions, and the coalescence of these forms the pattern by which a recent infection is easily recognized. In an infection of long duration this pattern may disappear and large areas of skin may present only an irregular scaling. The

Fig. 1.—The lesions are deeply stained by the method described, and the free scales have been removed.

scales may be attached to neighboring scales to form bands separated by dark-colored skin. On the hands the scales may be thick, large and yellowish and may be separated by furrows which are red but do not ooze serum. The skin of the plantar surfaces of the foot was exceptionally thick in the patients examined in this study. There may be longitudinal grooves in the nails, which are thickened and of ash gray color, with a raised border. The skin is abnormally dry except in the presence of eczematoid lesions. In the latter case there is regional adenopathy.

Besides the classic type of tokelau four variations were observed in this series: a diffuse type in which the annular pattern is not evident,

the East Indian type in which scales are widely separated by normal skin, a desquamative type with early shedding of the scales and a mixture of the three types.

The disease must be differentiated from ichthyosis, dermatitis exfoliativa, mal del pinto, favus, syphilis, pityriasis rubra grave of Hebra-Jadassohn and other types of dermatophytosis.

Tokelau is most common near the coast in the warm humid climate of tropical countries, but in Guatemala it appears to be more frequent in a region located from 80 to 170 kilometers from the Pacific Coast at an altitude of 3,000 to 5,000 feet (900 to 1,500 meters). It rarely develops in children younger than 10 years of age. In Guatemala it is more common in women than in men and is seen in rural peasants.

Fig. 2.—Lesions on the upper part of the chest and abdomen stained by the gentian violet method described. The duration of the lesions was six years.

Predisposing factors appear to be poor personal hygiene and deficient diet.

The patients with tokelau studied in this investigation were all workers in the Finca Santo Tomás P. in the state of Solalá. This finca is on the northwest slope of the volcano Atitlan, 93 kilometers from the Pacific Ocean. The altitude is 4,200 feet (1,260 meters), the average temperature is 19 C. (66.2 F.), the annual rainfall is high, and the humidity is above 85 per cent. The population of the finca numbers 210, and tokelau was observed in 11, of whom 8 were women. All those infected were native laborers, who live in crowded, small, thatched houses. Although they live in close proximity to domestic animals, the mycosis was not observed in the latter. The diet consists of beans, rice,

tortillas and coffee, with rare additions of meat and bread. The potable water has a low iodine content (goiter zone).

In order to facilitate photography of the lesions they were prepared by a method recommended by Dr. Horacio Figueroa. The lesions were rubbed vigorously with a compress saturated with 10 per cent gentian violet. On the following day the patient was instructed to bathe, taking care not to rub off the scales. The scales retain the stain while the intervening skin is decolorized.

In the isolation of the fungus the lesions were cleansed by rubbing for two minutes with a 60 per cent solution of alcohol. After the lesion was dry the scales were scraped with a sterile, dull scalpel into a sterile labeled test tube. For microscopic examination the scales were placed with the lower side up on a microscope slide in a drop of 40 per cent

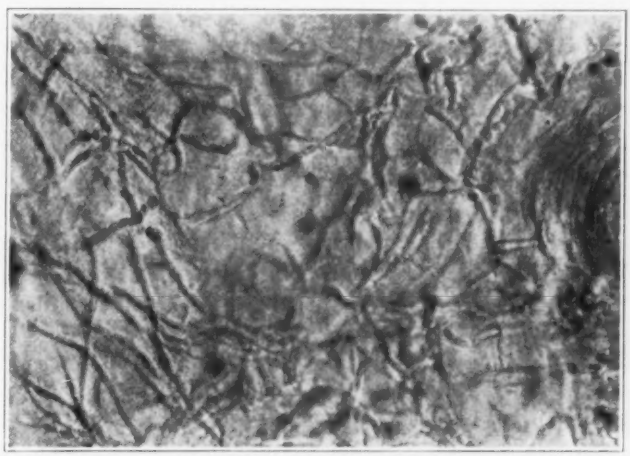

Fig. 3.—Appearance of the hyphae in scales.

solution of potassium hydroxide (a 10 per cent solution is equally effective) or in lactophenol and covered with a cover slip. Scales were also treated for forty-eight hours with the clearing medium of Oliveira Castro, which has the following composition: 60 cc. each of absolute ethyl alcohol and distilled water, and 240 cc. of chemically pure phenol crystals. Add 1 sq. cm. of Kodak carmine paper to each of 10 cc. of the clearing fluid.

In the scales septate hyphae of the fungus are numerous, branching freely and running in all directions to form an easily demonstrated mycelium (fig. 3). They are of fairly uniform diameter, except that in older hyphae where there are many septums the individual cells may be slightly enlarged, imparting a beaded appearance. There are also occasional large cells from which hyphal branches radiate.

The fungus was isolated in culture on Sabouraud's agar (glucose 20 Gm., peptone 10 Gm., distilled water 1,000 cc., agar 18 Gm.) by the following method: Scales were placed in an 80 per cent solution of alcohol for fifteen minutes, dried between two sterile slides and planted on agar slants. The fungus grows slowly, at first forming a small, heaped-up, irregular colony. As the colony increases in size radial folds and furrows develop from the center and some colonies become cerebriform. There is a flat, thin peripheral zone in older colonies. The surface is covered with a short white mycelium, giving the colony a gray color.

In 7 of the cases studies of the blood were made. These showed in all cases a negative Wassermann reaction and an eosinophilia varying from 12 to 17.6 per cent. Examinations of the stools of 9 of the patients revealed one or more of the intestinal parasites: Uncinaria, Ascaris and Trichocephalus. It was not determined whether the eosinophilia was due to the mycosis or to the parasites.

Tokelau does not respond well to treatment. The recommended procedures were used in these cases without complete success. Because of its efficacy in other mycoses iodine was tested. One preparation, iodoxyquinolinsulfonate of sodium, showed considerable promise and merits further trial.

SUMMARY

Eleven cases of tokelau occurring in the indigenous population of one finca in Guatemala were studied in detail. The mycosis appeared in classic form. Treatment has been only partially successful.

PEMPHIGUS VULGARIS

Successful Results Following Transfusion with Blood from Persons Who Had Recovered from the Disease

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AND
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PEMPHIGUS vulgaris is a constitutional disease whose most obvious and diagnostic manifestations are in the skin, thus resembling the exanthems. In recent years the etiologic agent has been thought to be a virus, and reports have already been made [1] of the isolation of strains in 4 cases of the disease. The relation of the strains to pemphigus vulgaris had not been established when the reports appeared, but subsequent data, now in preparation for publication,[2] indicate that the RP strain of virus is the etiologic agent of the disease. It was accordingly felt that antibodies which would neutralize the virus would be present in the blood serum of persons who had recovered from the disease. Owing to the high mortality and relative rarity of occurrence of pemphigus vulgaris, such persons are few in number and difficult to find. In response to nation-wide appeals, however, 2 women were found whose blood was used for transfusions to 2 men seriously ill with pemphigus vulgaris.

In this paper are presented the case histories of the 2 women who had recovered from the disease and the 2 men who received blood from them.

REPORT OF CASES

A. *Cases of persons recovered from pemphigus vulgaris.*

CASE 1.—S. J., a married gentile woman aged 27, was born in Pennsylvania of Polish parents. On Aug. 28, 1944 she felt more than usually tired, and on the following day she complained of discomfort around the eyes and mouth and also in the genital region, accompanied with the appearance of small vesicles on the conjunctivas and lips. When she awoke on the morning of August 30, there was considerable edema of the vulva and a generalized eruption which consisted

From the Long Island College Hospital and the Departments of Dermatology and Syphilology and Medicine, Long Island College of Medicine.

1. Grace, A. W., and Suskind, F. H.: An Agent, Transmissible to Mice, Obtained During a Study of Pemphigus Vulgaris, Proc. Soc. Exper. Biol. & Med. **37**:324, 1937; An Investigation of the Etiology of Pemphigus Vulgaris, J. Invest. Dermat. **2**:1, 1939.

2. Grace, A. W.: The Etiologic Agent of Pemphigus Vulgaris, to be published.

of "red spots with little blisters in the center." By 10 p. m., September 2, the oral temperature had risen to 104 F. and there were erythematous, macular lesions—some of which had small vesicular centers—in the conjunctivas and nasal orifices, on the lingual and buccal mucosae and in the vulval and perianal areas. The most distressing symptom was soreness in the mouth. During the next two days, a further development was the appearance of large bullae on the arms, legs, trunk and chin, the temperature meanwhile remaining at 104 F. On the morning of September 5, she was desperately ill and was seen by a dermatologist, Dr. Harry Saunders, who made the diagnosis of pemphigus vulgaris. The temperature began to fall on September 6, but an accurate measurement was not possible, owing to the extreme discomfort of the mouth and anus. Next day the temperature was normal, but the cutaneous lesions were bleeding and malodorous and had to be covered with dressings until September 15. Two days later she was allowed to get out of bed, and she was discharged from the hospital on September 24, at which time the lesions of the mucous membrane had disappeared and the skin was normal except for slight scaling in several areas. In a review of the internal and external medications employed in the treatment of the patient no substance was discovered which could be incriminated as the cause of the illness. There was no relapse between the time of the patient's discharge from the hospital and the first visit for the purpose of this study, on June 21, 1945.

CASE 2.—D. T., a married Jewish woman, was born in Minsk, Russia, in 1900. She became ill in New York city in 1921, a few hours after eating a meal of fried mushrooms. The initial picture was that of an acute gastrointestinal upset with diarrhea, vomiting and cramps in the abdomen. Two days later, when the gastrointestinal symptoms had subsided, the gums became covered with a "white film" which soon extended to involve the throat, tongue and mouth. This was followed by ulceration of the involved areas, especially the tongue. The disease smoldered in the mouth for the succeeding six months, during which time one area of the mucosa would heal and another would break down. At the end of that time, without any change in the condition of the mouth, the lips and vulva became edematous. Numerous exposures to ultraviolet rays were given as a therapeutic measure to the lips and vulva and had the effect, according to the patient, of spreading the disease to the boundaries of the irradiated skin, thus producing oozing, crusted, edematous, erythematous, confluent lesions on the circumoral areas and the upper inner portion of the thighs. With the exception of denudation of the skin of the umbilicus, no other portion of the integument was involved. At the height of her illness she was seen by Dr. L. D. Bulkley, who made a diagnosis of pemphigus. The disease persisted in the mouth for approximately one year and in the circumoral area for another six months, a total duration of illness of about eighteen months. During that period there was little elevation of temperature, and the weight fell from 146 to 80 pounds (66.2 to 36.3 Kg.). In a review of the internal and external medicaments employed in the treatment of the patient none was found which could be incriminated as the cause of the disease. There was no relapse between the time of the subsidence of the cutaneous lesions, in 1922, and the first visit for the purpose of this study, on June 26, 1945.

B. *Cases of persons sick with pemphigus vulgaris who received transfusions of blood from persons who had recovered from the disease.*

CASE 3.—H. W., a married Jewish man aged 54, was born in Poland. He was admitted to the Long Island College Hospital on March 26, 1945, after an

illness of eighteen months' duration, which illness began with "sores" in the mouth and later showed, in addition, blisters and crusted lesions on the skin and on the perianal areas. At the time of admission, the mouth and tongue presented numerous areas from which the mucosa was denuded, causing considerable soreness of the mouth. Similar areas of shallow ulceration were present in the perianal area. Collapsed pea-sized bullae with surrounding erythematous zones were found on the arms, legs, back and abdomen. There was no elevation of temperature. Treatment with penicillin was commenced, 40,000 Oxford units being given intramuscularly every three hours for a total of 6,960,000 units. With each of two of the daily doses of penicillin 6 cc. of human immune globulin (placental) was mixed and administered for a total of 216 cc. After this treatment had been given for nine days, the lesions began to dry and at the time of the patient's discharge from the hospital, on April 15, the skin was practically clear except for a small crusted area in the right inguinal region. The eruption in the mouth, however, was unchanged. For the next seven weeks H. W. resumed his business activities. He was hospitalized again on June 6, 1945, with lesions of the vegetating type in the inguinal and perianal areas. The general condition had deteriorated, and the temperature was 101 F. Treatment was resumed, with penicillin, immune globulin (placental) and Germanin, and during the period of treatment the involved areas in the mouth, the inguinal and the perianal regions increased in extent. Fresh crusted lesions appeared on the thighs, trunk, neck, chin and scalp, the temperature ranged between 101 and 102 F. and the general condition continued to deteriorate. On June 21 and on June 27 he was given a transfusion of 500 cc. of citrated blood, taken from S. J. and D. T., respectively. There was no untoward reaction to the receipt of the blood, nor had any improvement occurred at the time of the second transfusion. On June 30, however, the temperature fell to normal; all the cutaneous lesions began to dry and recede until by July 4 they had disappeared, leaving sharply demarcated, duskily erythematous flat areas at their former sites. The lesions in the mouth also cleared up. On July 4, a cerebral accident produced right hemiplegia and loss of speech. The skin remained clear until July 26, when small clusters of pinhead to matchhead sized pruritic vesicles appeared in the right inguinal region and on the right side of the scrotum. These clusters gradually extended, until, by August 24, palm-sized plaques of oozing granulation tissue were present on the upper inner aspect of both thighs and the scrotum and perianal area were involved with similar lesions. A transfusion of 500 cc. of citrated blood from S. J. was given, following which the cutaneous lesions began slowly to recede until by October 1 they had disappeared, leaving a flat, duskily erythematous residuum as before.

Case 4.—H. S., a married Jewish man aged 61, was born in New York city. He was admitted to the Long Island College Hospital on July 9, 1945, after an illness of six months' duration, which began with a cluster of vesicles in the left axilla and progressed with the formation of blisters and denuded areas on the limbs, trunk, mouth and perianal regions. At the time of his admission, the most striking lesion was a denuded, painful, oozing area 15 cm. in diameter on the upper right portion of the chest. Macerated epithelium was present in the mouth and perianal regions, and crusted lesions, some with concomitant collapsed bullae, were to be seen on the back, abdomen, inguinal regions and soles. From the day of admission the general and cutaneous conditions deteriorated. New bullae, bacteriologically sterile on aerobic and anaerobic culture, appeared in fresh sites at frequent intervals without diminution in the activity of older lesions. More than 60 per cent of the skin surface presented large raw, painful areas; the face was slightly edematous, and the appetite was impaired. No medication was given

until August 11 with the exception of sedation for pain and the application of boric acid ointment dressings on the cutaneous lesions to prevent them from sticking to the bed linen. On that date, when he was too weak to leave the bed, a transfusion was given of 500 cc. of citrated blood taken from D. T. Within twelve hours the systemic condition began to improve, and at the end of forty-eight hours the cutaneous lesions were less erythematous and less painful and were receding. On the fourteenth day after the transfusion all of the cutaneous lesions had been epithelized, and their sites were marked by sharply delimited, duskily erythematous, flat areas. On September 10 two crusted lesions, each 1½ inches (3.8 cm.) in diameter, appeared within the site of the large lesion which had been present on admission on the upper right portion of the chest. These new lesions persisted unchanged until October 10, at which time this report was compiled. At no time did the patient have any elevation of temperature.

COMMENT

It is impossible to escape the conclusion that the rapid disappearance of the systemic and cutaneous manifestations of both H. W. and H. S. was due to the blood transfusions which they received. Such blood, therefore, must be regarded as containing antibodies which neutralized, temporarily at least, the activity of the agent of pemphigus vulgaris. It is known that infections due to viruses may give rise to circulating neutralizing antibodies which can be demonstrated by protection tests for periods which, in the case of yellow fever, may be as long as sixty years after the acquisition of the disease. The relapses which occurred in both H. W. and H. S. can be regarded as being due to the low total amount of antibodies which they had received. When a sufficient number of persons who have recovered from pemphigus have been located, longer lasting therapeutic results will probably be achieved by transfusions of their blood at intervals of three or four weeks.

SUMMARY

The cutaneous and constitutional manifestations of pemphigus vulgaris in 2 persons seriously ill with the disease cleared rapidly after transfusion of blood from persons who had recovered from the disease.

SPOROTRICHOSIS WITH RADIATE FORMATION IN TISSUE

Report of a Case

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AND

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ST. LOUIS

RADIATE formation on cells of Sporotrichum was first observed by Splendore in 1908 and termed by him asteroid formation.[1] These star-shaped bodies were found extracellularly in pus obtained from a verrucous, vegetative, hard and somewhat elastic lesion, present for twenty days, on the right side of the face of an Italian woman living in São Paulo, Brazil.[2] Pure cultures of the fungus were obtained from this lesion and from two lymph nodes, the size of kidney beans, just beneath the primary site. The lesion began as a small button, increased in size gradually to take on the verrucous appearance and was a little pruritic. The nodes developed secondarily. The lesion cleared in a few days with potassium iodide taken internally and topical application of mild mercurous chloride ointment. The cultures were identified as Sporotrichum and because of the radiate formation of the cells in tissue a new species was created, Sporotrichum asteroides Splendore, 1908. The cultures were sent to de Beurmann and Gougerot, who considered the fungus a variety of Sporotrichum Beurmanni, S. Beurmanni var. asteroides (Splendore) de Beurmann and Gougerot, 1911.[3]

In 1907, Lutz and Splendore [4] described bizarre forms of organisms in man and in experimentally produced sporotrichosis in rats. In 1908,

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Studies, observations and reports from the Laboratory for Mycology of the Department of Dermatology of the Barnard Free Skin and Cancer Hospital, service of Dr. M. F. Engman, Sr., and from the Ellis Fischel State Cancer Hospital.

1. Splendore, A.: Sobre uma cultura de uma nova especie de cogumello pathogénico do homen, Rev. Soc. sc. de São Paulo **3**:62, 1908.

2. Splendore, A.: Sporotrichoses américanas, Brasil-med. **23**:361, 1909.

3. de Beurmann, L., and Gougerot, H.: Les sporotrichum pathogènes: Classification botanique, Arch. de parasitol. **15**:5, 1911.

(Footnotes continued on next page)

Greco [5] described radiate formation of Sporotrichum in man and rats from Argentina. In 1909, in France, Harter and Gruyer [6] described radiate formation in a guinea pig experimentally infected with Sporotrichum, supposedly S. Beurmanni (S. Schencki).

In 1934, Bordes, Berhouet and Errecart [7] published a report of 4 cases of sporotrichosis from Uruguay. During the course of the microscopic examination of sections from 1 of these cases (a gummatous lesion), Talice noted in the hematoxylin and eosin-stained preparation the asteroid formation described by Splendore. This case and another from Uruguay were published by Talice in 1935.[8] In the same publication there appeared a report on the production of radiate forms in experimental sporotrichosis of the rat by MacKinnon. At the meeting of the Third International Congress for Microbiology held in New York in September, 1939, MacKinnon [9] reported that he and Talice had found the asteroides form of Splendore in the pus from 6 of 7 patients with sporotrichosis. They also reported finding radiate forms in rats infected with a European strain of S. Schencki.

The presence of radiate or asteroid formation on cells of Sporotrichum, therefore, is not an unusual occurrence, but it is still sufficiently uncommon to warrant interest. To date, these structures have been found chiefly in man in South America-Brazil, Uruguay and Argentina —and in experimentally infected animals in South America and in Europe-France. The literature in North America as far as we know has not to date revealed this peculiar phenomenon.

REPORT OF CASE

History.—G. G., a white man aged 53, a construction worker, was admitted to the Ellis Fischel State Cancer Hospital on Dec. 14, 1944 with a complaint of a "sore" on the left hand of fourteen months' duration. He was born and

4. Lutz, A., and Splendore, A.: Sobre uma mycose observada em homens e ratos: Contribuição para o conhecimento das assim chamadas sporotrichoses, Rev. med. de São Paulo, Reprint, 1907; Sopra una micosi osservata in uomini e topi: Contribuzione alla conoscenza delle costi dette sporotrichosi, Ann. d'ig. sper. **17**: 581, 1907.

5. Greco, N. V.: Biologia del Sporotrichum Schenckii-Beurmanni: Etiologie y patogenia de la esporotricosis, Rev. dermat. **1**:78, 1908.

6. Harter, A., and Gruyer: Formes actinomycosiques dans la sporotrichose expérimentale, Compt. rend. Soc. de biol. **61**:309, 1909.

7. Bordes, C.; Berhouet, A., and Errecart, L. M.: Cuatro casos de esporotricosis, Bol. Soc. med. quir. del Centro de la Republica **7**:17, 1934.

8. Talice, R. V.: Deux cas de sporotrichose produits par le Sporotrichum astéroïde de Splendore, Ann. de parasitol. **13**:576, 1935.

9. Talice, R. V., and MacKinnon, J. E.: The Asteroides Form of Splendore in Spontaneous and Experimental Sporotrichosis, in Proceedings of Third International Congress of Microbiology (1939), 1945, pp. 510-511.

had lived in Missouri all his life. A small red spot first developed on the thumb where a crutch, used for a broken ankle, had rubbed. His physician applied "drawing salves," but the affected area increased in size and became hard and cracked. There was no ulceration, bleeding or itching. No other member of the family had any similar lesion. Three months prior to admission, two deep (subcutaneous) nodules appeared on the left arm. One month prior to entry a third nodule became apparent. Since that time several new nodules had been noticed. There had been no loss of weight or gastrointestinal symptoms. The past history revealed numerous operations and a "nervous breakdown" because of worry in 1934. There had been the usual childhood diseases and possible malaria and rheumatic fever, but the latter diseases had not been confirmed. The family history was irrelevant.

A systemic review revealed no symptoms relative to his eruption.

Physical Examination.—The patient was a well developed man, in no distress, weighing 155 pounds (70.3 Kg.). The blood pressure was 122 systolic and 74 diastolic, the pulse rate 72 and the respiration rate 20. On the skin of the chest

Fig. 1.—Verrucous, granulomatous lesion of the left thumb. The arrow indicates a subcutaneous nodule.

was a diffuse, symmetrically distributed, erythematous rash which blanched on pressure. Results of examinations of the eyes, ears, nose, throat, abdomen and other organs were not remarkable. Over the dorsum of the thumb of the left hand, in the region of the metacarpal and first phalanx was a hard, horny, raised lesion of the skin with irregular, verruca-like outgrowths (fig. 1). It measured 3 by 4.5 cm., was furrowed and cracked, but not ulcerated. The surrounding skin was intensely red and indurated. Extending up the forearm on the radial aspect were eight firm, rubbery, rounded areas of induration. These subcutaneous nodules did not appear beyond the elbow and were not painful or pruritic. Lymphadenopathy was absent. The clinical diagnosis was erythema nodosum.

Course.—The patient was discharged from the hospital on December 18, four days after admission, and was readmitted on December 26. The white blood cell count was 9,500 with a normal differential count. The Kahn test was negative. The agglutination test for tularemia gave negative results. A roentgenogram of the chest did not reveal any pulmonary involvement. A roentgenogram of the thumb showed soft tissue swelling, but no evidence of bone change. Biopsy specimens

were taken from the lesions on the thumb and wrist. Microscopic examination showed a granulomatous type of lesion suggestive of tuberculosis, syphilis, tularemia or fungous infection.

On Jan. 2, 1945 a nodule was excised. Part of the nodule was ground up and injected into a guinea pig, part was used for culturing and the remainder fixed, sectioned and stained for acid-fast bacteria. The guinea pig died but acid-fast bacteria were not found. A subsequent guinea pig inoculation with fresh material was also negative for Mycobacterium tuberculosis. The cultures were overrun with contaminants and no definite pathogenic fungus was isolated.

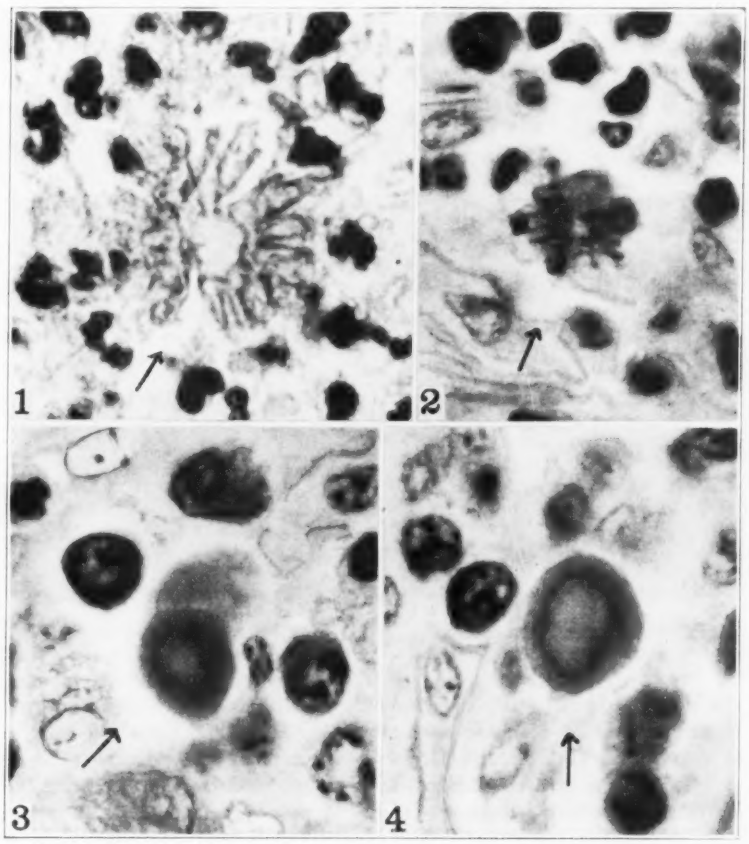

Fig. 2.—All photomicrographs made from a sporotrichotic nodule, stained with methylene blue and eosin, at a magnification of × 1520: *1*, asteroid form of Sporotrichum with a central, thick-walled cell surrounded by polymorphonuclear leukocytes; *2*, eosinophilic, radiate form with short rays; *3*, large pinkish blue-staining cell with eosinophilic material on the surface; *4*, single large bluish-pink cell of Sporotrichum.

Between January 4 and January 23, as an antiinflammatory measure, 800 r of roentgen rays was directed to the left thumb, 500 to the lower part of the left forearm and 500 to the upper part of the left forearm. The inflammation subsided somewhat, and on this basis a tentative diagnosis of Boeck's sarcoid was made.

The microscopic slides were submitted to one of us (M. M.) because of the possibility that the infection might be mycotic. Radiating forms were found having a central spherical cell and eosinophilic peripheral radiations. One of the structures in particular (fig. 2, *1*) bore a striking resemblance to that described by de Almeida [10] in experimental aspergillosis in the rabbit (see his fig. 11). Another node was excised for further study and for the cultivation of a pathogenic aspergillus. A review of the slides resulted in the diagnosis of sporotrichosis of the asteroid type. This was confirmed by the finding in culture of the characteristic Sporotrichum Schencki (S. asteroides).

On February 8 the patient was given a saturated solution of potassium iodide beginning with 10 drops three times a day. The dose was increased one drop daily, until on February 22 he was receiving 25 drops three times a day by mouth and topical applications of tincture of iodine. He gained 5 pounds (2.3 Kg.) in weight. The nodules on the forearm and the primary lesion on the thumb became progressively smaller. When seen in the clinic on March 28, the satellite nodules had almost disappeared and the involved thumb was practically healed except for slight crusting. He was told to continue the use of potassium iodide for two weeks. He was last seen on July 18. The thumb appeared well, but several barely perceptible nodules had again appeared over the left forearm. He was again given potassium iodide.

HISTOPATHOLOGIC OBSERVATIONS

The diagnosis having been established by culture, it was not difficult to recognize that histologically the picture was similar to that of the usual verrucous cutaneous sporotrichosis. The epidermis showed irregular acanthosis with an elongation of the stratum mucosum in some places and a shortening in other areas to produce a pseudoepitheliomatous formation. There was intercellular and intracellular edema, with a dense cellular infiltrate spread throughout most of the cutis. Scattered throughout the pseudoepitheliomatous growth in the cutis and extending into the epidermis was a prominent infiltrate of polymorphonuclear leukocytes forming microabscesses in some regions. The lymph spaces were dilated in the upper third of the cutis. In addition to the many polymorphonuclear leukocytes in the cutis there were plasma cells, young connective tissue cells, many epithelioid cells, lymphocytes, some scattered mast cells and giant cells of the Langhans type. Many small blood vessels were also seen throughout the infiltrate.

The presence of nodules in the tissue emphasized the granulomatous nature of the lesion. These nodules were usually deep in the cutis, but in some sections they were close to the epidermis. The individual nodules were characteristic of those usually seen in sporotrichosis. The central areas were made up of necrotic masses and in others small microabscesses could be seen. Surrounding the central area, usually termed the chronic suppurative zone, there were richly stained cells consisting

10. de Almeida, F. P.: Formacões radiadas da membrana dos cogumelos parasitos, Ann. Fac. de med. da Univ. de São Paulo **10**:163, 1934.

of polymorphonuclear neutrophils, some eosinophils, lymphocytes, red blood cells and some macrophages. Closely adjacent to this area were many epithelioid cells and giant cells of the Langhans type. The giant cells were variable in number, size and shape and occasionally appeared in groups suggesting a tubercle. This area corresponded to the tuberculoid zone. The outer or peripheral area of the nodule, the so-called syphiloid zone, was also characteristic of a typical sporotrichotic nodule, with plasma cells, connective tissue cells and lymphocytes. The blood vessels in the outer zone were small and increased in number. The collagen bundles were invaded by cells, chiefly lymphocytes and plasma cells. There was a perivascular reaction. Apparently as a result of the granulomatous process, the elastic fibers were irregular and broken so that the nodules appeared distinct. While many of the nodules were isolated, others were enlarged as a result of the merging of two or more nodules.

Of particular interest in the hematoxylin and eosin-stained sections were the radiating, acidophilic forms in the microabscesses of a nodule. With methylene blue and eosin these bodies appeared more distinctly as eosinophilic forms. The central cell was spherical and was surrounded by radiating, eosinophilic elongations (fig. 2, *1*). Scattered throughout the nodule, however, were acidophilic bodies varying in size and shape, some with short radiating structures and others without any peripheral additions (fig. 2, *2* and *4*). These scattered forms were usually surrounded by various cells, chiefly plasma cells and lymphocytes. The acidophilic bodies were identified as the asteroid form of S. Schencki.

MYCOLOGY

On the basis of radiate or asteroid formation of the cells in tissue, Splendore created the new species, S. asteroides, for the organism isolated from his case of sporotrichosis. De Beurmann and Gougerot and also Matruchot examined the culture, and although the fungus to them had all the characteristics of S. Beurmanni, they considered Splendore's organism as a variety, S. Beurmanni var. asteroides. The latter classification was arrived at by comparing the conidia, those of asteroides being more fusiform, and by considering the asteroid formation as a specific characteristic.

In tissue the fungus appears in two forms. The first is a short, somewhat rectangular basophilic cell measuring approximately 2 to 3 microns in its long axis. This form is similar to the cells found, but with much difficulty, in tissue of sporotrichosis when stained by the Gram method. Such cells were not seen in the tissue in the case presented herein. The second type has been designated as the asteroid form and is characterized by the presence in tissue or pus of radiate structures on the

pathogenic organism. In the tissue examined there were typical asteroid bodies having a central, spherical thick-walled (double-contoured), pink-staining cell, and measuring approximately 5 microns (some measuring 6 or 7 microns). Some of the central cells showed a blue coloration. The rays, eosinophilic staining, varied in length from 2 to 8 microns. Scattered throughout the nodule were acidophilic bodies varying in size from 6 to 12 microns, some of which appeared as young cells with short rays (fig. 2, *2*) while others were larger with a diffuse bluish pink color. Some of the large cells had diffuse pink material which appeared to be emanating from the wall of the cell (fig. 2, *3*). The radiate forms seen in the tissue were almost similar to those so well described by Splendore and also by Talice.

A portion of a biopsy specimen was planted on Sabouraud's glucose agar after the previous tissue implant had been overrun by contaminants. On the fourth day, although part of the agar slant was contaminated with saprophytic fungi, small dark brown to black colonies were seen. Isolated in pure culture, the fungus developed small cream-colored colonies which rapidly became black. Grossly, the growth was identical with that of S. Schencki (fig. 3, *1*). The center of the colony was irregularly convoluted to cerebriform. Radial grooves extended from the central formation, but not quite to the periphery of the growth. On glucose agar the cultures subsequently developed a dark brown duvet or powdery to somewhat cottony overgrowth, which is considered by some to be a pleomorphic change. This is in accord with the observations of de Beurmann and Gougerot.[11] Subcultures on other media likewise did not differ from those characteristic of S. Schencki.

Microscopically the cultural growth is made up of filaments and spores which closely correspond to the dimensions of those structures seen in S. Schencki (S. Beurmanni).[12] The hyphae vary from branched, interlacing, fine, threadlike, septate filaments, measuring approximately 1 to 2 microns in diameter, to pleomorphic types consisting of chains of oidioid or arthrosporous cells, approximately 3 to 5 microns in diameter. Large round cells with thick walls—chlamydospores—are seen as intercalary (within the hypha) or terminal structures measuring from 4 to 9 microns in diameter.

The conidia or spores are spherical, ovoid, pyriform or bacillary in appearance, pedicellate or sessile, occurring terminally or laterally, singly or in groups, measuring approximately 2 by 2 to 8 microns. When seen

11. de Beurmann, L., and Gougerot, H.: Les sporotrichoses, Paris, Félix Alcan, 1912, p. 140.

12. Moore, M., and Kile, R. L.: Generalized, Subcutaneous, Gummatous, Ulcerating Sporotrichosis: Report of a Case with a Study of the Etiologic Agent, Arch. Dermat. & Syph. **31**:672 (May) 1935.

in groups, they may take the form of a rosette or a cluster of spores on short branches, the spores being attached to sterigmata. When growing laterally the conidia appear to be directly attached to the hypha or connected by a short pedicle from which the spore, when mature, becomes easily detached. The young conidia are hyaline, thin walled and vary in shape and size, but when mature they tend to round up to form thick-

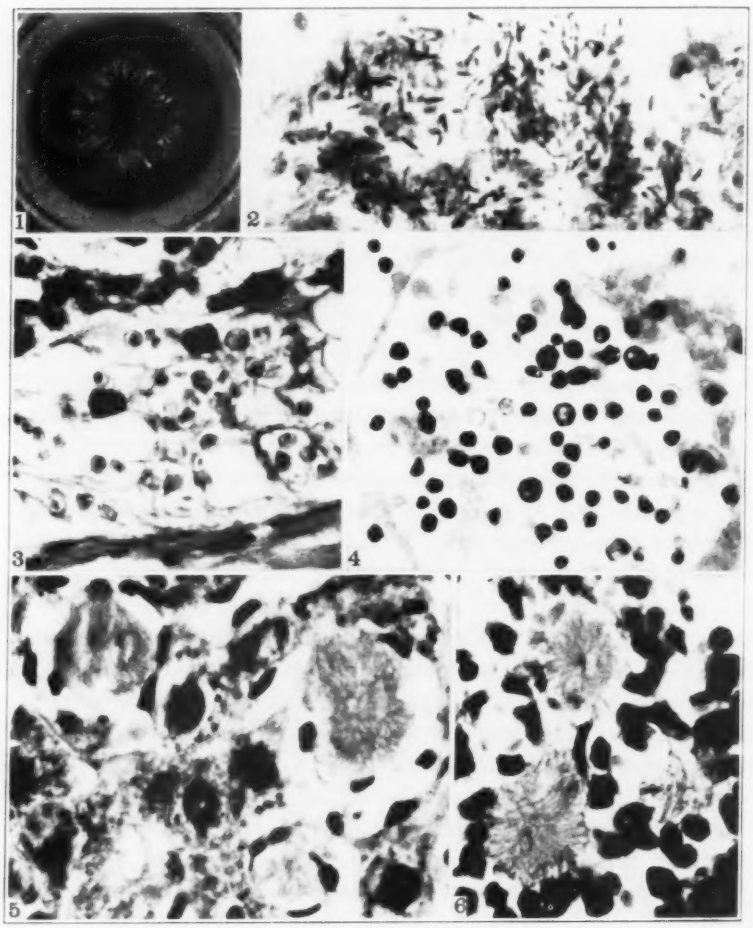

Fig. 3.—*1*, sixty day old subculture of Sporotrichum Schencki (S. asteroides) on Sabouraud's glucose agar; *2*, section of guinea pig tissue showing bacillary form of Sporotrichum—Gram-Weigert stain, × 754; *3*, section of mouse testis showing pink-staining spherical to ovoid cells of S. Schencki—hematoxylin and eosin, × 754; *4*, section of mouse testis showing spherical to ovoid simple or budding cells—Gram-Weigert stain, × 754; *5*, section of mouse liver with radiating forms in hepatic sinusoids—hematoxylin and eosin, × 677; *6*, section of mouse spleen showing radiating structures—hematoxylin and eosin, × 754.

walled spherical cells, usually brown, and measure approximately 4 microns in diameter.

Color is an important factor in species or at least variety differentiation. Such colors, however, in order to be of any value, should be constant or at least consistent with the strain of fungus. De Beurmann and Gougerot,[3] using color formation on Sarbouraud's agar as a criterion, established three groups or types of organisms: alpha which shows little pigmentation, remaining white or light brown; beta, which develops a chocolate brown color; and gamma, which changes from gray to ebony black in four to five days. Although such changes in color do occur, they should not be considered as a system of classification since, as has been pointed out previously,[12] variations in the constituents of the medium will alter the color of the growth. The continued subculturing of Sporotricha on the same medium, such as Sabouraud's glucose agar, will also cause changes in color. Furthermore, a comparison of eight strains of Sporotrichum, some of which had been recently isolated while others had been in the stock collection for several years, showed all the color changes on the same medium indicated in de Beurmann and Gougerot's classification. All the strains when first cultured were black. This holds true both for S. Schencki and for the fungus described as S. Beurmanni.

A comparison was also made of the morphologic appearance of S. Schencki and of strains having the characteristics attributed to S. Beurmanni. Except for minor differences which can invariably be found in strains of the same species, there is insufficient evidence to consider them as separate and distinct species. It is felt, therefore, that since S. Schencki was the first strain described, S. Beurmanni should be considered as a synonym. S. asteroides has all the features to be found in S. Schencki (S. Beurmanni) with the addition of asteroid formation in tissue. Asteroid or radiate formation in tissue, although a rare phenomenon in sporotrichosis, is not uncommon with other organisms such as Actinomyces (most species), Coccidioides immitis, Aspergillus fumigatus and others. In view of the fact that radiate formation of fungi is merely a concomitant finding in tissue and not an expression of species differentiation, it is felt that such a finding is not sufficient reason in itself for designating this strain of Sporotrichum as a new species or even as a variety. Consequently, this organism should be S. Schencki.

Sporotrichum Schencki Matruchot, L.: Compt. rend. Acad. d. Sc. **150**:543, 1910.

Synonymy: Sporotrichum sp. E. F. Smith in Schenck: Bull. Johns Hopkins Hosp. **9**:286, 1898.

Sporothrix Schencki Hektoen, L., and Perkins, C. F.: J. Exper Med. **5**:77, 1900.

Sporotrichum Beurmanni Matruchot and Ramond: Compt. rend. Soc. de biol. **57**:379, 1905.

Sporotrichum asteroides Splendore, A.: Rev. Soc. sc. São Paulo **3**:62, 1908; Brasil-med. **23**:361, 1909.

Rhinocladium Beurmanni var. asteroides Vuillemin, P.: Compt. rend. Acad. d. sc. **21**:148, 1910.

Sporotrichum Beurmanni var. asteroides de Beurmann, L., and Gougerot, H.: Arch. de parasitol. **15**:42, 1911.

Rhinocladium Beurmanni Vuillemin, cited by de Beurmann, L., and Gougerot, H.: Arch. de parasitol. **15**:98, 1911.

Sporotrichopsis Beurmanni Guéguen, cited by de Beurmann, L., and Gougerot, H.: Arch. de parasitol. **15**:103, 1911.

Rhinotrichum asteroides Verdun, P.: Précis de parasitologie humaine, Paris, G. Doin, 1912; Verdun, P., and Mandoul, A. H.: ed. 3, ibid., 1924, pp. 714-715.

Sporothrix asteroides Davis, D. J.: J. Infect. Dis. **12**:453, 1913.

Rhinocladium Schencki Verdun, P., and Mandoul, A. H.: Précis de parasitologie humaine, ed. 3, Paris, G. Doin, 1924, pp. 713-714.

Rhinotrichum Schencki Ota: Jap. J. Dermat. & Urol. **28**:4, 1928.

Rhinotrichum Beurmanni Ota: Jap. J. Dermat. & Urol. **28**:4, 1928.

Rhinocladium Schencki Grandinetti, L.: Contribução para o estudo da esporotricose, São Paulo, Empr. Rev. tribunais, 1934, p. 18.

Rhinocladium asteroides Grandinetti, L.: Contribução para o estudo da esporotricose, São Paulo, Empr. Rev. tribunais, 1934, p. 53.

Sporotrichum Schencki var. Beurmanni (Matruchot and Ramond) Dodge, C. W.: Medical Mycology, St. Louis, C. V. Mosby Company, 1935, p. 806.

ANIMAL INOCULATIONS

A ground-up, excised, subcutaneous nodule was injected intraperitoneally into a guinea pig. Death followed nine days after injection. Sections of tissue stained by the Gram-Weigert method revealed clumps of the short, somewhat rectangular cells of Sporotrichum occurring as individual or occasionally as joined cells (fig. 3, *2*).

A saline suspension of organisms made from a twelve day old subculture on Sabouraud's glucose agar was injected into 2 mice, 1 male and 1 female. It was injected intraperitoneally into the female and intraperitoneally and intratesticularly into the male. The male died one hundred and forty-three days following the injections, but the female was still alive after one hundred and eighty-two days. Autopsy was performed on the male mouse. Grossly there was no apparent change in most of the organs of the thoracic and abdominal cavities. The testes, however, were greatly enlarged and covered with small tubercle-like protuberances. Microscopically, there were necrotic nodules of varying size in

the testes. The centers of the nodules showed liquefaction necrosis and were made up of leukocytes, most of them in a degenerative state. The periphery of the nodule was made up of fibroblasts and then fibrosis. Scattered throughout the nodule, especially prevalent in the areas of liquefaction and arranged for the most part in clumps, were large numbers of spherical, simple or budding yeastlike cells, measuring from 4 to 8 microns in diameter. In sections stained with hematoxylin and eosin these cells were pink or eosinophilic (fig. 3, *3*). In the methylene blue and eosin sections, the central area of the cell appeared blue, whereas the wall took the eosin stain. When stained by the Gram-Weigert method, the yeastlike organisms were deep purple (fig. 3, *4*). No radiate or asteroid forms were seen in the testes.

The lungs and kidneys did not contain organisms. In the liver there was an infiltrate of leukocytes in areas around the margin. In the hepatic sinusoids there were radiating structures of various sizes (fig. 3, *5*). It was difficult to determine with complete satisfaction whether these bodies represented the typical asteroid forms of sporotrichosis. These bodies were eosinophilic, but no central fungus cell similar to that seen in human tissue or to those seen in the testes could be found by various staining procedures. The radiations did, however, appear to emanate from the central region. The spleen appeared somewhat larger than normal. Microscopically, there were many areas of necrosis, especially evident close to the capsule. Radiating forms similar to those seen in the liver were found in the spleen (fig. 3, *6*). The radiations here too seemed to emanate from the central region of the structure. Several nodes taken from the mediastinal region did not appear normal, but microscopically they showed only inflammation.

SUMMARY AND CONCLUSIONS

A case of granulomatous, verrucous sporotrichosis of the left thumb with a subsequent lymphatic spread in the form of subcutaneous nodules is presented. Microscopically, sections of nodules were characteristic of sporotrichosis. The finding of acidophilic, radiating structures in a nodule of the tissue at first suggested aspergillosis. The cultivation of a Sporotrichum, however, established the diagnosis of sporotrichosis with asteroid formation in tissue. The fungus, first named Sporotrichum asteroides by Splendore, then S. Beurmanni var. asteroides by de Beurmann and Gougerot, when studied in detail, appears similar to, if not identical with, strains of S. Schencki. On the basis of comparative studies with eight strains of Sporotrichum, it was concluded that the strain showing the radiate structures in tissue should be classified as S. Schencki. Asteroid formation was not observed in a guinea pig into which tissue was injected. Instead, the characteristic bacillary form was

seen in tissue sections stained by the Gram-Weigert method. In a mouse into which was injected a suspension of organisms from a twelve day old subculture of the fungus, ovoid to spherical, simple or budding, yeast-like cells were found in the testes. Radiate structures were found in the liver and spleen, but their nature was not definitely ascertained. Because of the finding of radiating structures on fungi in other diseases, it may be concluded that asteroid formation in sporotrichosis should be considered as a concomitant, although uncommon, finding. The finding of such structures in tissue is insufficient reason in itself for the establishment of either a different species or a different variety.

CONTACT DERMATITIS

An Analysis or Tabulation of All Cases Proved In a Single Year

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IN human beings, eczematous dermatitis is possibly the most common of all recognized allergic diseases."[1] It is an entity which may be caused by many unrelated substances. In our private practice Dr. Bedford Shelmire and I kept notes for a period of one year on all patients with contact dermatitis in whom the offending allergen or allergens were discovered. The purpose of this paper is to present the unusual features of a few of these cases, to point out the common sensitizing substances found to be peculiar to some specialized trades, and to emphasize the frequent occurrence of sensitization dermatitis from topical medications.

All cases presented represent proved examples of eczematous contact dermatitis. In each case the opportunity for exposure to the substance or substances was demonstrated; an eczematous reaction followed patch tests with harmless concentrations of the material in question and elimination of the substances which elicited the positive reaction resulted in a disappearance of the dermatitis. A large number of patients seen during the same period of time unquestionably had contact dermatitis but could not be included in this series because all the previously mentioned postulates could not be fulfilled.

None of the numerous instances of dermatitis venenata from poison ivy are included or is any attempt made to show statistically the place of eczematous contact dermatitis in relation to other dermatologic disorders. During the twelve month period, we were able to prove the cause of contact dermatitis in 250 cases.

CONTACT DERMATITIS FROM TOPICAL APPLICATIONS

The cause of eczematous contact dermatitis was found to be topical medicaments more frequently than any other single group of allergens. Some estimation of the likelihood of sensitization from specific drugs can be obtained from a summary (table 1) of the proved cases. Sulfonamide compounds and mercurials in topical application rank as the most potent sensitizing agents and therefore the preparations most likely to

1. Sulzberger, M. B.: Dermatologic Allergy, Springfield, Ill., Charles C Thomas, Publisher, 1940, p. 89.

cause contact dermatitis. If a person is sensitized to merthiolate for example, he may or may not be found to be allergic to ammoniated mercury and/or mercury bichloride. He, therefore, may be sensitive to only a few or to many of the mercurial drugs. On the other hand, if a patient is sensitized to sulfathiazole, he is likely to be hypersensitive to other sulfonamide preparations.

TABLE 1.—*Contact Dermatitis from Drugs*

Drugs	Number of Cases
Mercurials	
Ammoniated mercury	14
Mercury bichloride	3
Oleate of mercury (mercresol)	2
Merthiolate	2
Mild mercurous chloride (dusting powder)	1
Solution of merbromin	1
Neko soap (potassium mercuric iodide)	1
Mercuric salicylate	1
Total	25
Sulfonamide compounds	
Sulfathiazole ointment	19
Sulfadiazine ointment	2
Sulfanilamide (powder)	3
Total	24
Tars	
Solution of coal tar	5
Crude coal tar	4
Total	9
Resorcinol	5
Benzocaine—contained in Foille; Derma Medicone; Korium, and Calagesic ointment	4
Butesin picrate	4
Quinolor	2
Nupercaine hydrochloride	2
Other drugs and preparations	
Hydrophen (orthophenylmercuric nitrate)	1
Acetarsone (powder)	1
Butacaine sulfate	1
Sulfur (ppt.)	1
Metycaine hydrochloride	1
Calmitol	1
Mazon	1
Zemo lotion	1
Tannic acid	1
Resinol ointment	1
Prescription (active ingredients: resorcinol, phenol, juniper tar)	1
Formaldehyde	1
Total	12

An interesting feature of sensitization to tars presented itself. It was observed that patients who become sensitized to crude coal tar were also hypersensitive to solution of coal tar. The reverse is also true, except for the rare possibility that a person using solution of coal tar will become sensitized to the vehicle alcohol or the quillaja rather than to the coal tar. Solution of coal tar contains: coal tar, 200 Gm.; quillaja, in moderately coarse powder, 100 Gm.; and alcohol in sufficient quantity to make 1,000 cc.

Sensitization dermatitis from topical medicaments following the treatment of some trivial eruption, as pruritus, miliaria, a superficial

burn, an insect bite, poison ivy dermatitis, sunburn or "athlete's foot," is a common and everyday occurrence. When contact dermatitis occurs during the course of topical chemotherapy, the common mistaken interpretation is that infection, such as erysipelas or cellulitis, has occurred or that the patient has contracted poison ivy dermatitis.

The following case summaries are included to illustrate sensitization dermatitis from the topical application of drugs.

CASE 1.—On the seventh postoperative day following a herniorrhaphy in the right inguinal region, both the surgeon and the patient noted a slight erythematous swelling and weeping at the site of the healing wound. A serous drainage was observed on the dressing. A diagnosis of infection was entertained, and a 10 per cent solution of merbromin was applied twice daily. During the next three or four days the dermatitis became more intense and covered a wider area than before. On examination of the operative site, the eruption was found to involve an ever widening rectangular area which conformed exactly to the site being treated with merbromin. It was apparent that the patient was allergic to this substance. Merthiolate had been used to prepare the skin before operation. Unquestionably, that application was the sensitizing exposure, because a seven day interval, the period of incubation of sensitivity, preceded the onset of this eruption. Patch tests elicited positive reactions to both merthiolate and merbromin. The dermatitis healed rapidly after the use of merbromin was discontinued.

CASE 2.—J. H. was given chlorohydroxyquinoline ointment for local application to a small area of folliculitis on the back of the neck. At the end of ten days' treatment, the eruption had improved only slightly. A 6 per cent bismuth tribromphenate ointment was then prescribed. This was applied for twenty-four hours, and the following morning an acute contact dermatitis of the neck was noted by the patient. He was greatly displeased, thinking that the new ointment was "too strong." From his history, it was learned that he had never used bismuth tribromphenate or chlorohydroxyquinoline before. Patch tests with these two preparations elicited a strongly positive reaction to the latter and a negative one to the former.

This case illustrated an example of sensitization dermatitis in a patient who was in the process of acquiring sensitivity to chlorohydroxyquinoline (in the incubation period of sensitization) when a new drug was started. Obviously stopping the drug at that point would not have prevented the development of the allergic reaction.

CASE 3.—C. M. C., a truck driver, received a superficial cut on the dorsum of the right hand and the fourth and fifth fingers. Sulfanilamide powder was used locally for approximately nine days. At this time an erythematous and finely vesicular dermatitis appeared over the treated sites. The physician, observing the hand at this period, made a diagnosis of cellulitis. Hot wet compresses alternated with sulfathiazole ointment were prescribed. The eruption progressed to involve the lower half of the forearm and the exposed parts of the face, neck, ears and left arm. In this patient there developed both a sensitization and a general photosensitivity to sulfonamide compounds. He also exemplified group sensitization, being hypersensitive to both sulfanilamide and sulfathiazole.

Use of patch tests with sulfonamide drugs on patients who are sensitive to the compounds is not without danger, especially in persons who

are photosensitive. Because of our previous experience with several cases of accentuation of existing eruptions which followed positive reactions to patch tests, contact testing with sulfonamide drugs was largely discontinued before this study was started. We have found that

TABLE 2.—*Contact Dermatitis Due to Occupational Allergens*

Occupation	No. of Cases	Areas Involved	Allergens
Worker preparing carrots for dehydration	1	Hands, forearms	Carrots
M.D., general practice	1	Fingers	Procaine hydrochloride
M.D., surgeon	1	Hands	Rubber gloves
Worker in aircraft industry	1	Hands, forearms	Rubber gloves
Highway construction: bridges, etc., working with lumber treated with creosote	1	Face, hands, forearms	Creosote
Construction worker contacting posts and telephone poles treated with creosote	1	Face, neck, chest, arms	Creosote
Workers in aircraft industry contacting plastics	4 1	Face, arms, hands Face, arms, hands	Formaldehyde Phenol formaldehyde resin
Workers in aircraft industry contacting plywood	3	Hands, forearms	Glue (possible formaldehyde sensitivity)
Aviator	1	Ears	Rubber earcup
Baker	1	Fingers, hands	Cinnamon
Worker in aircraft industry	1	Face, neck, eyelids, hand	Naptha
Tinter of photographs	1	Tips of fingers: 1, 2, 3 left hand	Turpentine
Men dipping lumber in a chemical solution called "sealer" before shipping to tropics	2	Hands, arms, ears, face, neck	"Sealer"
Dental technicians who prepare false dentures	1 1	Finger tips Finger tips	Carbon tetrachloride Ethylene glycol
"Car hop" at root beer stand. Glasses and mugs were dipped in chlorine solution for cleaning	1	Hands, forearms	Chlorine
Worker in industry, manufacturing tents for military use	1	Hands, forearms, face	Olive drab cloth
Workers for cleaning and polishing Greyhound Bus Company	2	Hands	Johnson cleaner
Workers in blueprint industry, manufacture of ice	7	Hands, face, eyelids	Bichromate
Workers in aircraft industry	10	Hands, face, neck, forearms, eyelids	Zinc chromate primer
Farmers, ranchers, oil field workers	35	Exposed areas; face, legs, arms	Weeds
Worker washing containers into which honey was extracted	1	Hands, face, neck, forearms	Honey and beeswax
Nurses, housewives	3	Hands, face, eyelids	Primrose plant
Barber	1	Backs of hands, fingers	Bay rum
Housewife	1	Hands, arms, face	Citronella
Housewife	1	Face, neck, forearms	Flit
Housewife	1	Right hand, lips, eyelids	Cocobolo wood

the oral administration of a small dose (1 grain [0.06 Gm.]) of the sulfonamide drug in question is serviceable in proving specific sensitization. Positive reactions to patch tests were noted in this series in only 2 of our 23 cases, and proof of sensitivity was confirmed by oral test doses in 2

other cases. In 9 cases the reactions were recorded as unquestionable sensitization to sulfonamide compounds and in 10 other cases as eruptions most likely due to sulfonamide compounds.

CONTACT DERMATITIS OF OCCUPATIONAL ORIGIN

There are many occupations in which persons are exposed to the hazard of contact dermatitis (table 2). In the Southwest, eczematous contact dermatitis from sensitization to vegetation is a common occurrence (table 3). This type of eruption is not a disease affecting solely one occupation, yet contact dermatitis from weeds must be considered an

Fig. 1.—Contact dermatitis in aviator, from rubber ear cups.

occupational hazard among farmers, ranchers, workers in the oil fields and others. Persons living solely in large metropolitan areas rarely have dermatitis from weeds. Those who have contact with weeds only infrequently may become hypersensitive, however. A severe widespread eczema due to weeds was observed in a banker who had contact with vegetation only while hunting, fishing and golfing. One of our patients with a most extensive eruption was a man whose occupation was that of sheriff. Two cases have been observed in which the patients were ministers who held services in rural areas during the summer months. Another patient is a dentist whose hobby is cattle raising. He makes contact with vegetation while riding horseback to inspect his herd on week ends and after office hours.

TABLE 3.—*Reactions to Patch Tests with Oleoresins of Weeds*

Weed	Case Number																																	Total
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	
Iva angustifolia (Narrow-leaved marsh elder)	+	+	+	..	..	..	+	+	..	+	..	..	..	..	+	..	+	..	..	..	..	..	+	+	+	+	+	+	..	+	+	..	..	+	+	18
Helenium tenuifolium (Bitterweed)	+	+	+	..	..	..	+	+	..	+	+	+	..	+	..	+	+	+	..	..	..	..	..	+	+	..	+	+	+	+	+	..	..	..	+	20
Ambrosia elatior (Short ragweed)	+	+	+	+	+	+	+	+	+	+	+	..	..	+	+	..	+	..	+	+	..	..	+	+	+	+	+	+	..	..	..	..	..	..	+	23
Helenium microcephalum (Sneezeweed)	+	+	+	..	..	..	+	+	..	+	+	+	+	+	..	+	+	..	..	..	+	..	..	+	+	+	..	..	..	+	+	..	+	..	+	20
Parthenium hysterophorus (Santa Maria feverfew)	+	..	+	+	+	..	+	+	+	+	+	..	..	+	+	..	+	+	+	+	+	+	+	..	+	+	+	+	..	..	..	+	..	..	+	24
Xanthium speciosum (Cocklebur)	..	..	..	..	..	..	+	+	..	..	..	..	..	..	..	..	..	..	..	..	+	..	+	+	..	..	..	..	..	..	..	..	..	..	+	6
Iva axillaris (Lesser marsh elder)	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Pyrethrum	+	..	..	..	..	..	..	..	..	..	..	..	..	+	..	..	..	..	..	..	+	..	+	+	..	..	..	+	..	..	..	..	..	..	+	3
Ratibida columnaris (Coneflower)	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Medicago hispida (Bur clover)	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Agrostis alba (Red top)	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Grindelia squarrosa (Gumplant)	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Artemisia mexicana (Common wormwood)	+	..	..	..	..	..	..	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2
Eupatorium serotinum (Boneset)	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Chenopodium botrys (Jerusalem oak)	+	..	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2
Acuan illinoensis (Illinois mimosa)	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Amphiachyris dracunculoides (Broomweed)	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Amaranthus blitoides (Prostrate amaranth)	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Amaranthus retroflexus (Red root pigweed)	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Solidago serotina (Late goldenrod)	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1
Thelesperma gracile (False coreopsis)	+	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1

| | | |

The history of the course of a dermatitis from weeds is usually easily obtained and is characteristic. The eruption frequently commences on the areas of the ankles, with an onset usually in early spring. As the season progresses, the backs of the hands, forearms, face, eyelids and neck become involved. The eruption may progress to involve the entire exposed surfaces of the body. After frost kills all the vegetation, the eczema slowly clears. The patient usually remains well throughout the winter months. Acute exacerbrations during this period have been seen from contact made with weed-contaminated hay and other foodstuffs. The dermatitis reappears with the return of vegetation in the spring. Each year the eczema becomes more extensive; subjective symptoms are more annoying, and the dermatitis requires a longer time to clear after the vegetation dies. The diagnosis "ragweed dermatitis" should be reserved for those in which a sensitivity to ragweed alone is demonstrated. A polyvalent sensitization occurs more frequently than hypersensitivity to a single weed. An example of an unusual case of polysensitivity to weeds was that of a rancher who was found to give positive contact reactions to forty different weeds (case 1, table 3). Only five reactions were strongly positive. The others were definite but mild. The slight reactions may be interpreted as evidence of minimal sensitivity to those specific plants. Continuous contact with those particular weeds would probably result in a mild eczematous dermatitis.

In cases of sensitization dermatitis due to weeds, only two methods of management are possible. These are (1) absolute avoidance of vegetation and (2) hyposensitization with the specific weed oleoresins. In persons who can avoid vegetation by giving up some hobby, as golfing or hunting, or in others for whom change of occupation is possible, the dermatitis will clear completely and remain well. The majority of persons in whom dermatitis due to weeds develops are farmers and ranchers who cannot avoid vegetation if they carry on their work. The oral administration of specific weed oils to understanding cooperative persons has proved to be of unquestioned value in the majority of our cases. Enough protection is afforded by this method of increasing one's tolerance to allow a continuation of the patient's occupation. The specific oleoresins should be taken during the winter months and repeated yearly.

The following are unusual cases of contact dermatitis of occupational origin. Rare examples of dermatitis from vegetation, usually occupational, are those from woods, vegetation oils and extracts.

The primrose plant blooms from December through March. It is often presented as a floral gift to hospitalized patients, as a birthday greeting and on other special occasions, such as Valentine's Day. Contact dermatitis from the primrose plant is said to occur frequently among florists. Morphologically, primrose and ivy dermatitis are indistinguish-

able. I should like to point out that dermatitis venenata from the primrose also occurs frequently in nurses and housewives.

CASE 4.—Mrs. F. M., a housewife, made a habit of pouring water with her right hand into a pot containing a primrose plant, while she protected the blossoms by bending the flowering portion of the plant to one side. The dead leaves and stems were pruned with the fingers of her left hand. A unilateral vesicular eruption of

Fig. 2.—Contact eczema of upper lip and right palm, from cocobolo wood (case 5).

the fingers and the palm resulted. The striking resemblance of this eruption to dyshidrosis was noted. Proving the diagnosis of dermatitis due to the primrose is usually easily done by employing an extract of primrose for patch testing or by lightly streaking a crushed leaf on a suitable test site. The unusual feature of this case was the limitation of the eruption to the lateral margins of the fingers and palm of the left hand.

Case 5.—Mrs. J. K. consulted us because of a recurrent eczematous dermatitis involving the eyelids and perioral sites and a healing vesicular dermatitis of the fingers and palmar surface of the right hand. Acute attacks of this eruption occurred while the patient was away from home as well as while at home. Absolutely no clues regarding the cause of this eruption could be got from a lengthy conversation with the patient. She had discontinued use of nail lacquer, hair tonics, wave sets, all cosmetics, drugs (local and oral) and perfumes. Patch tests for sixty common flowers, seven weed oleoresins and six drugs commonly employed in topical medications elicited negative reactions. A twenty-four hour covered patch test, a small quantity of cocobolo wood shavings being used, produced a vesicular response on the right forearm. A focal flare-up involving the eyelids and circumoral sites and the right hand, characterized by an erythema, edema with fine vesiculation and pruritus occurred. The eruption became severe enough to necessitate continuous wet compresses and confinement to bed for several days.

This patient apparently became sensitized to cocobolo wood by contacts with knife handles made of this wood, which she used in her kitchen. When away from home she frequently contacted this allergen because she often ate steak and was

Table 4.—*Contact Dermatitis from Wearing Apparel*

Item	Number of Cases
Nickel (rings, jewelry, glasses, underwear snaps, strap adjusters, etc.)	6
Khaki clothing	2
House shoes	1
Brown nylon sox (real silk brand)	1
Sox supporters (leather portion)	1
Stockings of nylon (redyed)	1
Glasses (plastic slip-on temple piece)	1
Miscellaneous contact allergens	
Matches	1
Toilet seat	1
Adhesive tape	1
Green dye in patch testing set of common vegetables	1
New golf glove	1

given a heavy steak knife with a cocobolo wood handle. She has remained well since avoiding knives with cocobolo wood handles.

Case 6.—J. S. presented a typical contact dermatitis of two weeks' duration, involving the face, eyelids, neck, arms and hands. The eruption had the appearance of a dermatitis from weeds. A similar eruption had been experienced six months prior to the present attack. The patient worked in a plant where honey from different parts of the United States was collected, the honeycomb extracted and the syrup blended for marketing. He contacted both the honey and beeswax (honeycomb) daily. The honey being extracted at the time of the present dermatitis was from Iowa. Patch tests with the Iowa honey and beeswax elicited strongly positive reactions, while tests on two controls elicited negative reactions. This man was found to react only to Iowa honey. Contact tests with honey from three other localities elicited negative reactions. Patch tests were made with oleoresins from sixty common flowers and one hundred and twenty different weeds in an attempt to find out whether the patient was allergic to pollen or to some plant substance transported to the honey by the bees. No positive reactions to the plant oils were obtained. Investigation of company records revealed that honey collected from Iowa was being extracted and blended at the time of the patient's first attack of eczema, several months prior to the present eruption.

CASE 7.—H. B., a barber by trade, consulted me because of chronic eczema on the fingers of both hands. At his first visit, he brought for testing purposes approximately thirty different materials that he commonly used. They included several brands of hair tonics, shampoos, powder, creams, shaving and hand lotions, bay rum, etc. All patch tests elicited negative reactions, except the test with bay rum, which was found to elicit a consistently positive reaction. This solution

Fig. 3.—Contact dermatitis on finger tips of dental technician, due to ethylene glycol.

Fig. 4.—Dermatitis venenata, from adhesive tape used for sprained wrist.

was used by the barber in a lotion which he applied to his hands after frequent washings. Discontinuing the use of the hand lotion brought about a permanent remission of the eczematous eruption.

Two similar cases of eczematous contact dermatitis in barbers from this cause were encountered approximately one year before. Bay rum

should be considered a frequent cause of contact dermatitis of the hands in barbers.

Case 8.—Mrs. M. C., a dentist's assistant, was seen with a chronic fissured and thickened eczema of the finger tips, involving chiefly the right thumb, index finger and middle finger. The patient spent much of her time in helping to prepare artificial dentures. Patch tests were made with the various materials used in preparing false teeth. Hypersensitivity to carbon tetrachloride was demonstrated. The eruption cleared slowly, and the patient recovered completely after a substitute for carbon tetrachloride was employed.

A second dental technician was seen with an eczema of the finger tips of both hands. The sensitization dermatitis was proved to be due to

Table 5.—*Sensitization Dermatitis from Cosmetics*

Cosmetics	Number of Cases
Nail polish (clear and colored)	20
Hair lacquer	
Hubére lacquer (pads)	21
Lacquer (spray)	
Nutrine brand	3
Renée	2
Henri Maison	2
Wavelak	1
Total	29
Lipstick (dye)	1
Eyelash dye	
Roux brand	1
Brand unknown	1
Total	2
Shampoo (Fitch)	1
Chamberlain's Lotion	1
Harriet Hubbard Ayer Skin Lotion	1
Ra-Lo Lotion	1
Tussy's Cold Cream	1
Hair rinse (brand unknown)	1
Cold permanent wave (Helené Curtis Preliminary Solution)	1

ethylene glycol which was used in the preparation of artificial dentures. Avoidance of this chemical in his work resulted in the cure of the patient's eruption.

Case 9.—J. F., a truck driver, presented a pruritic eczematous eruption on the greater portion of the entire body. The face and hands were uninvolved. Thickened weeping areas were noted over the base of the neck posteriorly, in the axillas and popliteal regions and along the waist line. After approximately two or three months' observation, the possibility of khaki clothing as a cause of this dermatitis was considered. A forty-eight hour patch test with khaki elicited a questionable positive reaction. The patient was hospitalized for seven days, and his dermatitis improved strikingly. A khaki shirt was then worn part of one day. The eczematous eruption reappeared over the areas contacted by the shirt. The patient has remained well since substituting other work clothing for khaki.

Case 10.—E. B., a cafe owner, while being treated for pyoderma of the hands, requested an investigation to determine whether he was hypersensitive to lettuce

or tomatoes. Patch tests, using 1 drop of an extract of tomatoes and of lettuce, were made. The solutions employed were part of a commercial set of vegetable extracts. A fine vesicular eruption appeared at the sites where the test patches with the two extracts were applied. Contact tests with fresh lettuce and tomatoes elicited negative reactions. A search was made for the reason of the false positive reactions to the lettuce and tomato extracts. It was learned that acetone was used as a vehicle in preparing the vegetable extracts, and a small quantity of green dye was incorporated to mark the site of the test. The patient was found by patch testing to be hypersensitive to this green dye. A similar incident of sensitivity to the green dye in the set of weed extracts had been observed two years earlier.

News and Comment

Vacancies in the United States Public Health Service.—Appointments to fill vacancies in the Reserve Corps of the United States Public Health Service are now being made, and examinations for appointments to the Regular Corps will be held in April and May, Surgeon General Thomas Parran announced today.

Pay and allowances, established by law, are identical with those for medical officers of the Army. All traveling expenses, including travel to the first station, are paid by the Service.

In announcing the recruitment campaign, Dr. Parran stated that the opportunities for professional growth and development are almost limitless. There is clinical work in Public Health Service hospitals throughout the country. Opportunities for research exist in both laboratory and field.

Appointments to the Reserve Corps are made on a basis of review of data furnished by the applicant. Physical examination is required.

Appointments to the Regular Corps require appearance before a Board and a written professional examination. Dates and places for the examination will be announced shortly.

Those interested either in immediate appointment in the Reserve Corps or in taking the examination for the Regular Corps should request application forms from The Surgeon General, United States Public Health Service, Federal Security Agency, Washington, D. C.

American Academy of Dermatology and Syphilology.—The American Academy of Dermatology and Syphilology will hold its next meeting on Dec. 8 to 12, 1946, in Cleveland, Ohio.

Applications for membership can now be made. Dermatologists wishing to apply for membership may secure necessary information by writing to the secretary, EARL D. OSBORNE, Secretary, 471 Delaware Avenue, Buffalo, N. Y.

CORRECTION

In the article by Dr. Erich Urbach and Dr. John W. Lentz entitled "Carbohydrate Metabolism and the Skin" in the November-December issue (ARCH. DERMAT. & SYPH. **52**:301, 1945) the words "blood" and "skin" in the heading of the third column of table 1 were inadvertently transposed. The heading should read "Skin/Blood Sugar Ratio."

KERATOSIS BLENNORRHAGICA

Its Response to Penicillin

MAJOR RICHARD EMMET
Medical Corps, Army of the United States

A SEARCH of the available literature reveals no record of the use of penicillin in the treatment of keratosis blenorrhagica. For this reason it seems desirable to report a case in which intramuscular injection of penicillin was followed by cessation of all symptoms and clearing of the cutaneous lesions.

REPORT OF A CASE

History.—A white soldier, 21 years old, single, was admitted to the Station Hospital on Feb. 1, 1944, complaining of a painful foot and pain and swelling of the left knee. His previous history was not remarkable, except that he had been treated with sulfadiazine for gonorrhea on an ambulatory basis from Jan. 5, 1944 to January 10. The pain in the foot and the swelling of the knee followed a hike of 5 miles (8 kilometers). The patient reported to the infirmary and was sent to the Station Hospital with a diagnosis of a possible march fracture.

Clinical Examination.—There were no abnormalities except considerable effusion in the left knee and pain and stiffness on deep bending of the knee and pes planus, second degree, with slight flattening of the metatarsal arch. The temperature was 99.4 F., and the pulse rate was 100. Roentgen examination of the foot did not reveal fracture.

Diagnoses.—The working diagnoses were: (1) second degree symptomatic pes planus, (2) acute traumatic nonsuppurative synovitis of the left knee, secondary to continued walking on the side of the foot during a march, (3) rheumatic fever and (4) acute infectious arthritis.

Course.—The patient was treated with rest in bed and hot packs to his knee, with almost complete recession of the effusion in the knee joint. Six days later, on February 7, a urethral discharge was noted. The smear was positive for gonococci, and the patient was given sulfadiazine. He received 12 Gm. in the first twenty-four hours and then 1 Gm. every four hours day and night for nine more days. The discharge continued, however, and after several days of rest he was again given 12 Gm. of sulfadiazine in twenty-four hours, followed by 1 Gm. every four hours day and night for four more days. The urethral discharge stopped. Meanwhile, however, the pain in the knee continued, and on February 28 swelling of the right wrist was noted. At this time his temperature ranged from 98.6 to 100 F. The white cell count was 12,300, and the sedimentation rate was 100 mm. per hour. He was transferred to the arthritis ward and given salicylates by mouth and heat was applied to his knee. The impression was that he had an acute infectious arthritis. The disease continued, and by the middle of March, six weeks after admission, the pains in the joints were becoming migratory, involving both knees and the left ankle, right hand and the right wrist. On March 20 bullae were noted on both knees and were considered by the ward officer to be toxic erythema.

More vesicles and bullae appeared, and some of the older ones became pustular and then crusted. On March 29 I was called to see the case in consultation. On the feet, legs and thighs, in decreasing order of severity, on the lower part of the abdomen and on the forearms and hands were many vesicles and pustules, and large numbers of discrete hornlike lesions, varying from 0.5 to 3 cm. in diameter. The hornlike character was particularly noticeable on the toes and feet. Tenderness and swelling of the left knee joint were present. When some of the crusts were pulled off, a grayish pink, slightly oozing surface was noticed. The diagnosis of keratosis blennorrhagica was readily made. A biopsy specimen was taken from one of the lesions of the foot for confirmation, and the histologist, Major Ralph C. Ellis, reported as follows:

"The specimen consists of a roughly oval portion of skin measuring 12 by 9 mm. in size. In the central portion there is an area 7 mm. in diameter in which

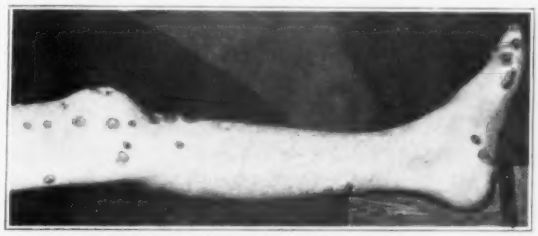

Fig. 1.—Keratosis blennorrhagica, just prior to administration of penicillin. Note effusion of knee joint. (Photograph by U. S. Army Signal Corps.)

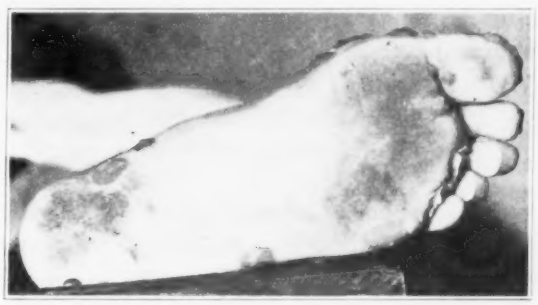

Fig. 2.—Just prior to administration of penicillin. (Photograph by U. S. Army Signal Corps.)

the superficial layer has been split off and has separated from the underlying skin. Attached to this area at one side is a cone-shaped top of keratinized material which is almost completely separated from the skin. Microscopic section shows a portion of the skin with extensive hyperkeratosis and parakeratosis near the center. A thick keratinized cap has separated from the central portion and is seen separately. It contains large numbers of nuclei and portions of polymorphonuclear leukocytes. In the remaining intact skin there is one small vesicle-like space between the epithelium and the underlying keratin. The epidermis itself is hyperplastic, with branching, proliferating pegs extending downward in the superficial dermis. In the superficial epidermis the cell outlines are loose and large numbers of polymorphonuclear leukocytes are seen embedded within the epithelium. The dermis contains many inflammatory cells, chiefly mononuclear in

type. They are scattered diffusely beneath the epidermis, although at the lateral margins they have a perivascular arrangement."

The diagnosis was keratosis blennorrhagica.

Prostatic massage was done but the smear showed no gonococci. It did, however, contain many polymorphonuclear leukocytes. Some of the hornlike nodules on the skin were removed, and smears were made from their bases but did not show any gonococci.

On April 3 the patient was given penicillin intramuscularly, the initial injection being 40,000 units, followed by 20,000 units every three hours for a total of 200,000 units (twenty-four hours). No local treatment, not even soap and water, was used. Two days later new vesicles were still appearing, but on April 6 no further lesions were noted and those present began to dry and fall off. The articular pains became much less severe on April 7, and on April 11 the patient began to sit up in a chair; five days later he was walking around the ward, although with a little difficulty. On April 14 his temperature, which had been varying from 99 to 101 F., returned to normal, and remained that way. All lesions had disappeared by April 16. The patient was kept in the hospital, ambulatory, for one more month to regain his weight and the use of the muscles of his legs. He was then discharged to the reconditioning unit and was last seen on June 6, by which time he had completely regained his weight and had been making 15 mile (24 kilometers) marches without difficulty.

SUMMARY AND CONCLUSIONS

A soldier had keratosis blennorrhagica with all the classic features of gonorrheal urethritis. In a few weeks monoarticular arthritis appeared, together with a recurrence of the urethritis. This was followed by migrating polyarticular involvement associated with typical cutaneous lesions.

No gonococci were found in the cutaneous lesions, but they were recovered from the urethral discharge before treatment was begun with sulfadiazine.

Administration of penicillin intramuscularly without any local therapy caused cessation of all symptoms, including pyrexia, swelling of the joints and pain, and clearing of the cutaneous lesions. Although cultures for gonococci were not obtained, for technical reasons, the cure of the patient is presumed since there has been no recurrence for two months, even after hard physical exercise.

THEOPHYLLINE ETHYLENEDIAMINE AS AN ANTIPRURITIC AGENT

Preliminary Report

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OAKLAND, CALIF.

ALL dermatologists, in fact all practitioners, are confronted frequently by patients with severely pruitic eruptions that fail to respond to the usual therapeutic agents. Such patients are a burden to their physician, to their family and to themselves. Besides leading to loss of weight, severe psychoneuroses or other manifestations their ailment may even eventuate in suicide. Therefore this preliminary report is offered on the as yet imperfectly understood action of theophylline ethylenediamine in the immediate relief of generalized and localized itching. The results are so dramatic as to warrant extensive research on this subject.

Theophylline ethylenediamine has been employed by intravenous injection in the treatment of patients with asthma and other diseases since 1940.[1] Most authors feel that the use of the drug is safe when it is administered by this route. While the immediate symptoms, such as dyspnea, flushing, tachycardia and prickly sensations in the mouth and skin are disconcerting, serious complications due to administering the drug were not reported in human beings until 1943.[2]

TECHNIC OF TREATMENT

So far, theophylline ethylenediamine has been unquestionably and uniformly effective in relieving itching only when it is injected intravenously. The usual technic consists of the very slow injection of 0.5 Gm. of the drug in 20 cc. of fluid. The rate of injection can be controlled by the use of a 25 gage needle. The speed of injection can also be controlled by the incorporation of the dose in 1,000 cc. of 5 per cent or 10 per cent solution of dextrose. If this is done, the results are not as dramatic and not as uniform as those obtained with the syringe method, an aspect which will be discussed later in this report.

It should be emphasized that the injection must be given very slowly. The drug is dangerous when given intravenously, and speed shock must be avoided.

1. Herrman, G., and Aynesworth, M. B.: Successful Treatment of Persistent Extensive Dyspnea, "Status Asthmaticus," J. Lab. & Clin. Med. **23**:135 (Nov.) 1937; cited by Carr.[4]

2. Merrill, G. A.: Aminophylline Deaths, J. A. M. A. **123**:1115 (Dec. 25) 1943.

RESULTS

The method was first suggested to me by Kruetzer.[3] He told of treating a patient for bronchial asthma with the intravenous injection of theophylline ethylenediamine. The patient also had a severe poison oak dermatitis and noted immediate cessation of the itching. Kruetzer used this method to treat a number of other patients with itching eruptions, with good results. He was of the opinion that the relief of pruritus was greatest in patients with poison oak dermatitis.

This report is based on the results obtained in treating nearly 100 patients with various types of itching dermatoses. About 25 received treatment by the syringe method. In this group were included patients with various pruritic localized and generalized dermatoses, including poison oak dermatitis and other forms of contact dermatitis, eczema (disseminated neurodermatitis), exfoliative dermatitis and localized eczemas of the hands. Immediate relief of itching was noted in all cases. Occasionally there was little effect from the first injection but subsequent doses resulted in prompt cessation of the itching. The relief lasted for from thirty minutes to twelve hours, the average complete freedom from itching being about four hours. The recurrence of itching was seldom as severe as the preceding pruritus. No more than two injections were given in any twenty-four hour period. The objective cutaneous lesions responded much more rapidly once the physical and psychologic trauma of itching was relieved by this treatment.

Itching usually stops after the injection of 2 to 5 cc. of the solution. However, the full 20 cc. is administered. The dramatic suddenness of the relief makes a profound impression on both the patient and the physician.

The necessity for repeated injections and the possible complications to be discussed later make this agent more valuable against acute pruritus than against chronic types.

DANGERS

It would be foolhardy for any one to adopt this method without knowledge of the dangers involved. Carr [4] in 1940 mentioned a total of 55 cases from the literature and from his own experience in which this manner of treatment was used without difficulty. Sperling, Weisman and Papermaster [5] used this drug in 169 cases following operations on

3. Kruetzer, W.: Personal communication to the author.

4. Carr, H. A.: Treatment of Acute Attacks of Bronchial Asthma by the Intravenous Injection of Aminophyllin, J. Lab. & Clin. Med. **25**:1295 (Sept.) 1940.

5. Sperling, L.; Weisman, S. J., and Papermaster, R.: Effect of Intravenous Theophylline with Ethylene Diamine (Aminophylline) upon Rate and Depth of Respiration, Surgery **11**:600 (April) 1942.

the abdomen, without serious ill effects. Brown and Blanton [6] added 31 more cases of asthma treated with the same results. Unger [7] stated that he had treated hundreds of patients without difficulty. My results have been the same.

On the other hand, Luduena,[8] as the result of animal experimentation, came to the conclusion that theophylline ethylenediamine given intravenously might lead to meningeal and/or renal changes and therefore its administration should not be continued indefinitely. He did state, however, that he knew of a patient who had received two hundred injections of this drug over a period of two or three months without demonstrable difficulty.

Merrill [2] reported death occurring in 3 cases while the injection of theophylline ethylenediamine was being given. While all these patients showed evidence of serious heart disease, the fact that fatalities occurred while the injection was being given leaves no doubt that the drug was responsible for the deaths. Merrill mentioned 2 other deaths that he had heard of informally. I have been told of 2 other cases similar to the 3 reported by Merrill.

OTHER METHODS OF ADMINISTRATION

Theophylline ethylenediamine is ineffective as an antipruritic agent when administered orally, rectally or locally. The results have been somewhat beneficial when the drug was injected intramuscularly in doses of 0.5 Gm. in 2 cc. of fluid. Many patients experience relief of itching within thirty minutes, and this may persist for from hours to days, usually one to twelve hours. However, other patients fail to experience any benefit from the injection. Many patients also complain of numbness in the hip and/or the leg after the injection.

The incorporation of the 20 cc. ampule of the drug in 1,000 cc. of 5 per cent or 10 per cent dextrose decreases the toxicity. Unfortunately, the relief of itching is neither so dramatic nor so uniform as with the syringe method. In fact, 1 patient with pruritus ani suffered a severe paroxysm of itching after 600 of the 1,000 cc. of the solution had been administered by gravity.

Both the intramuscular and the gravity intravenous injections eliminate the immediate disconcerting symptoms. However, this is of little basic importance.

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6. Brown, A. G., III, and Blanton, W. B.: Therapeutic Effects of Aminophyllin in Asthma, South. M. J. **33**:1184 (Nov.) 1940.

7. Unger, L.: Aminophylline Deaths, J. A. M. A. **124**:320 (Jan. 29) 1944.

8. Luduena, F. P.: Bronchial Antispasmodic Actions of Theophylline Derivatives, J. Pharmacol. & Exper. Therap. **75**:316 (Aug.) 1942.

COMMENT

Sperling and his co-workers [5] demonstrated that the intravenous injection of theophylline ethylenediamine by the syringe method increases the depth of respiration by 51 per cent while the rate is 26 per cent faster after its administration. Unger [7] pointed out that the deaths occurred in patients with impaired cardiac reserve. These two facts possibly explain the mechanism of death. It is suggested that a patient whose cardiac condition is such that he cannot tolerate severe overexertion should not be given the drug intravenously.

It should be remembered that patients do not die from itching. While pruritus may be nerve racking, a drug with fatal potentialities should be used with great caution to alleviate this condition. Enthusiasm for the results must not obscure the dangers. Careful selection of cases is essential.

It is of interest to note the rapid healing that occurs when the itching is relieved.

This is merely a preliminary report to acquaint other clinicians with the dramatic possibilities of this drug. Further studies are being conducted in an effort to find a safer effective way in which to administer it.

SUMMARY

Theophylline ethylenediamine given intravenously by the syringe method in doses of 0.5 Gm. proved to be an effective antipruritic agent for various dermatoses. The relief occurred immediately and lasted for from thirty minutes to twelve hours.

The results of intramuscular and gravity intravenous injection of the drug were less dramatic and less constant.

There is a definite danger of death occurring in patients with impaired cardiac reserve who are given this drug intravenously by the syringe method.

Further studies are being conducted to find a safer effective route of administration.

BLUE NEVUS OF JADASSOHN AND TIÈCHE

Report of a Case

MEYER L. NIEDELMAN, M.D.
PHILADELPHIA

THE following case of blue nevus is reported because of the unusual size of the nevus, its rapid growth and clinical characteristics of a melanoma.

A blue nevus [1] resembles a melanoma but it is bluish gray or blue-black, round or oval and slightly elevated. It is firm to palpation and is most frequently situated on the face or on the extensor surfaces of the extremities. It is usually benign but occasionally undergoes sarcomatous changes. Clinically, the blue nevus of Jadassohn and Tièche may easily be confused with benign pigmented nevus, pigmented basal cell epithelioma and melanoma.

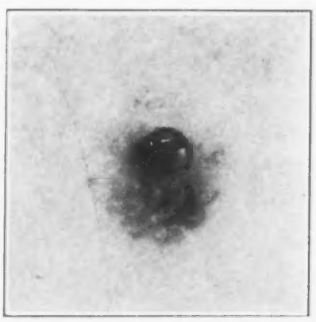

Fig. 1.—Blue nevus of Jadassohn and Tièche showing features indistinguishable from melanoma. Note the unusual size.

REPORT OF CASE

History.—H. M., an American housewife aged 40, complained of a rapidly growing black mass on the left shoulder. She stated that she remembered always having a small wart in the brassiere strap area on the left shoulder. In the last six months, this had rapidly grown to the dimensions seen when she presented herself. Examination showed two elevated circumscribed lesions about ⅜ inch (0.96 cm.) in diameter situated on a dark base. The lesions were hard and bluish black. There were no subjective symptoms. The lesions clinically resembled a melanoma (fig. 1).

1. Farrell, H. J.: The Cutaneous Melanomas, Arch. Dermat. & Syph. **26**:110 (July) 1932.

The entire lesion was excised by the cutting current, and the base was thoroughly desiccated. As there was a remote possibility that the lesions might become malignant, the area was given roentgen ray therapy with 600 r, unfiltered, twice weekly for three weeks.

Biopsy Report (Dr. Fred Weidman).—The portion of the specimen selected for histologic study came from a part of the lesion which was only superficially

Fig. 2.—Section from blue nevus showing close resemblance to melanoma. Pigmented cells extend from the base of the ulcer to the level of the sweat glands.

ulcerated. The epidermis was highly acanthotic in all its parts except at the site of the superficial ulceration. There was not the slightest evidence of malignant change in it. The basement membrane was closely scrutinized for the presence of Langerhans cells, but none were found. Accordingly, the pigmented lesion in the corium scarcely could be a dermoepidermal nevus.

In the center of the section there was a fairly well delimited region of pigmented tissue. It extended from the base of the ulcer almost to the level of the sweat glands but did not attain the plane of surgical excision. Within this region the collagenous bundles were widely separated by smaller and larger masses of a pigmented "tumor." The tumor had a matrix that was only slightly vascular but loosely fibrillar. On it there were great numbers of cells laden with melanin.

The pigmented cells did not have the characters of those of malignant melanoma or of a dermoepidermal nevus. In the first place, although the shape of the cells varied from spindle to polyhedral, they were relatively uniform in size. Too, they were remarkably uniformly and invariably crowded with the pigment granules—something that is inconsistent with malignant melanoma. Again, the nucleus was invariably round and relatively small. There was not any of the clustering of cells that occurs in malignant melanoma. All of these features are compatible with those of the blue nevus.

HISTOLOGIC SUMMARY

The patient presented a remarkably large, highly projecting and ulcerated example of a blue nevus. There is not the slightest difficulty in vetoing a diagnosis of a dermoepidermal nevus which has undergone malignancy. The possibility has been considered whether the exceptional clinical features could be explained on the basis of malignant transformation of a blue nevus, exceptional though it is. The sections do not permit this assumption; at no place were the nuclei of the character to allow that idea to be entertained. In short, the lesion could be nothing but a blue nevus in spite of its most exceptional clinical features.

COMMENT

A woman had an unusually large blue nevus of Jadassohn which clinically resembled a melanoma. The microscopic examination of the lesion was paramount to a diagnosis, as all of these lesions present certain common characteristics and similarities.

500 Central Medical Building.

Obituaries

ALFRED POTTER, M.D.
1880-1945

Alfred Potter, a graduate of the Long Island College Hospital in 1902, died on Dec. 27, 1945, after a brief illness, at the age of 65. His medical career had been long and active. After graduation he interned

ALFRED POTTER, M.D.
1880-1945

at the Long Island College Hospital for two years and followed this with postgraduate training in dermatology at Columbia University as well as in bacteriology and in syphilology at the Rockefeller Institute. In his

early days of practice he was a diagnostician in the Department of Contagious Diseases, for the Department of Health, New York City. He resigned this position in 1913 to devote himself entirely to the practice of dermatology and syphilology in Brooklyn.

He served his alma mater well for many years, first as instructor in dermatology and then as professor of dermatology from 1920 to 1930. In the latter year he became emeritus professor of dermatology.

He had been honored with appointments to the dermatologic staffs of many hospitals, either as an attending physician or as a consultant. Among them were the Long Island College Hospital, Jewish Hospital, Harbor Hospital, House of St. Giles for Cripples, Bikur Cholin Hospital, Swedish Hospital, Samaritan Hospital, Home for Destitute Children, Brooklyn Eye and Ear Hospital, Norwegian Lutheran Deaconesses' Home and Hospital and Lutheran, Mary Immaculate, Jamaica, Brooklyn State and Englewood (N. J.) Hospitals. At the Kings County Hospital he served continuously from 1908 as attending dermatologist and syphilologist until 1941, when he became consultant to this service. He was the director of this department from 1923 until 1941.

Dr. Potter was a member of the Kings County Medical Society, American Medical Association, Brooklyn Medical Association, Associated Physicians of Long Island and the Hospital Graduates Club. He was also a member of Montauk Lodge 268, Free and Accepted Masons. He had been a member of the New York Dermatological Society and the Tenth International Congress of Dermatology and Syphilology. He was certified by the American Board of Dermatology and Syphilology in the founders group.

His contributions to dermatologic literature were published in *The Journal of the American Medical Association, Journal of Cutaneous Diseases, Long Island Medical Journal* and the *International Journal of Surgery*.

He was a lover of the outdoors, particularly of the sea, and spent much of his time golfing, walking and swimming. During recent years he established his summer home at Guilford, Conn.

Surviving him are his wife, Beatrice, a daughter, Mrs. John Taylor, a brother, Henry A. Potter, and two sisters, Mrs. J. R. Carpenter and Mrs. George Bailey.

E. ALMORE GAUVAIN, M.D.

HARRY BAILEY, M.D.
1898-1946

Dr. Bailey was born in New Haven, Conn., Aug. 10, 1898, the son of Charles and Fanny Schwartz Bailey. He attended New Haven public schools and was graduated from Yale University in 1919 and from the University of Maryland School of Medicine and College of Physicians and Surgeons in 1922. He interned at St. Francis' Hospital, Hartford, Conn., and did graduate work in dermatology at the New York Post-Graduate Medical School and Hospital, 1930 to 1931.

He was a member of the Yale Naval Medical Unit and a veteran of World War I.

He was chief of the dermatologic service at Mount Sinai Hospital and at Municipal Hospitals, Hartford, and was a member of the executive board of both hospitals. He was also chief of dermatology at the Hartford Dispensary. He was a fellow of the American Academy of Dermatology and Syphilology, the American Medical Association, the Hartford Medical Society and of the New England Dermatological Society. He was a former chairman of the dermatologic section of the Connecticut State Medical Society and was a specialist certified by the American Board of Dermatology and Syphilology, Inc.

He was also a member of Temple Beth Israel, the Masons, the American Jewish Congress and the Zionist Organization of America.

Dr. Bailey died on Jan. 12, 1946, rather suddenly after a short illness prior to which he had been in excellent health. Besides his parents, who live in New Haven, he leaves his wife, the former Eva Waxman, whom he married in 1932; a daughter, Susan Gail Bailey; a sister, Mrs. Ernest Gladstone, of New York city, and a brother, Manning Bailey, of New Haven.

Dr. Bailey gave generously of his services, often sacrificing his health and personal pleasures for the welfare of his patients. He was highly esteemed and loved by his patients, friends and associates. His willingness to aid at all times, his conservative, sound judgment, his conscientious thoroughness and his genial nature will well be remembered and missed by all who knew him.

E. M. S.

Correspondence

TYROTHRICIN IN CUTANEOUS INFECTIONS

To the Editor:—Dr. Harold E. Anderson published a paper (Tyrothricin in Cutaneous Infections, ARCH. DERMAT. & SYPH. **53**:20 [Jan.] 1946) containing serious technical mistakes which have led him to erroneous deductions. In addition, he makes assumptions which are not justifiable. The method he used in testing the activity of tyrothricin in the ointment bases was ill chosen. His results only confirm the well known fact that tyrothricin is insoluble in isotonic solution of sodium chloride and do not show that tyrothricin is inactivated by the ointments. Substances of macroscopic size, which are completely insoluble in water, simply do not diffuse through agar. If Dr. Anderson had used any of the following applicable methods with the cetyl alcohol formula, he would have found full activity of the tyrothricin: (1) microscopic checking of growth or viable counts of susceptible organisms inoculated into serial dilutions of the tyrothricin ointment in fluid thioglycollate medium or broth (Difco brain-heart) with or without added serum or bovine albumin; (2) dilution of the ointment with serum or albumin agar in Petri dishes and streaking with susceptible organisms; (3) mouse protection test with Pneumococcus type I. In a personal communication, Dr. Dubos has said this in vivo method is the most reliable one for the assaying of gramicidin or tyrothricin.

Further, Dr. Anderson suggests that the components of tyrothricin react with the ingredients of the ointment bases, leading to inactivation. Such a reaction is not consonant with the nature of these substances; it is partially at variance with previously published data (Dubos, R. J., and Hotchkiss, R. D.: Origin, Nature and Properties of Gramicidin and Tyrocidine, Tr. & Stud., Coll. Physicians, Philadelphia **10**:11-19 [April] 1942). Our unpublished work indicates that the apparent reduction of the activity of tyrothricin in the presence of fats, fatty acid esters, etc., is a matter of solubility. Tyrothricin is more soluble in these substances than in water.

E. J. FOLEY, M.D., and S. W. LEE, PH.D., Princeton, N. J.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

A STUDY OF THE TYPES OF HYPERSENSITIVITY INDUCED BY PENICILLIN. ADOLPH ROSTENBERG JR. and HENRY WELCH, Am. J. M. Sc. **210**:158 (Aug.) 1945.

After finding an instance of hypersensitivity of the tuberculin type to crystalline penicillin sodium in a person who had had no previous contact with this drug, the authors made a study to determine the incidence of this type of sensitivity. It was found that 5 per cent of 144 persons tested with crystalline penicillin sodium exhibited a positive reaction of the tuberculin type despite the fact that none had had any prior contact with penicillin. It was postulated that there had been previous ingestion or inhalation of spores of Penicillium.

Rostenberg and Welch showed that the reactions obtained following intradermal injection of penicillin sodium fall into two categories. In the spontaneously sensitive persons all reactions were of the tuberculin type. In the persons originally without sensitivity but who became hypersensitive after repeated intradermal injections of penicillin sodium, the reactions, although eventually developing into a tuberculin type of hypersensitivity, were transiently wheal-like before this stage was reached.

OSTEOMYELITIS CAUSED BY GRANULOMA INGUINALE: REPORT OF A CASE WITH CULTIVATION OF THE DONOVAN BODY IN THE YOLK SAC OF THE DEVELOPING CHICK EMBRYO. WALTER H. SHELDON, BEN R. THEBAUT, ALBERT HEYMAN and MARGARET J. WALL, Am. J. M. Sc. **210**:237 (Aug.) 1945.

Skeletal or visceral manifestations of granuloma inguinale have rarely been noted. In the case reported by Sheldon and his associates there were characteristic cutaneous lesions, one on the penis and a larger one on the leg, which surrounded an ulcer which extended into the medullary cavity of the tibia. Donovan bodies were found in histologic sections from this case and were cultivated in the yolk sac of developing chick embryos. Since the patient stated that the ulcer appeared on the leg nine weeks before the appearance of the penile lesion, the authors concluded that the ulcer on the leg might represent a primary extragenital lesion with secondary contact infection of the penis or that the lesion on the penis was present at the same time as the ulcer on the leg, but was too small to be noticed by the patient.

GENERAL ACQUIRED ANHYDROSIS. HUGO T. ENGELHARDT and J. P. MELVIN JR., Am. J. M. Sc. **210**:323 (Sept.) 1945.

Englehardt and Melvin state that acquired anhidrosis is even rarer than congenital ectodermal dysplasia without ability to sweat. They report a case in which a patient with general acquired anhidrosis is described. Various diagnostic procedures verified this diagnosis. Histopathologic examination of sections of skin revealed generalized atrophy of the sweat glands. With experimental modification of temperature and humidity the authors were unable to induce sweating in their patient, being able to collect only a small amount of fluid, which they egarded as resulting from simple diffusion.

DIFFERENTIAL ROLES OF LAYERS OF HUMAN EPIGASTRIC SKIN ON DIFFUSION RATE OF WATER. TRAVIS WINSOR and GEORGE E. BURCH, Arch. Int. Med. **74**:428 (Dec.) 1944.

RATE OF INSENSIBLE PERSPIRATION (DIFFUSION OF WATER) LOCALLY THROUGH LIVING AND THROUGH DEAD HUMAN SKIN. GEORGE E. BURCH and TRAVIS WINSOR, ibid. **74**:437 (Dec.) 1944.

The rates of diffusion of water through living and through dead human skin were measured in an attempt to determine the portion of the skin mainly responsible

for inhibiting diffusion and preventing excessive loss of water from the body. Winsor and Burch found that the corium is the most important layer of the skin in inhibiting the diffusion of water. They noted that the rate of diffusion of water through dead and through living skin is virtually the same. It is noted that most observers of insensible perspiration have failed to distinguish between the part of water lost insensibly through secretions of the sweat glands and that part lost through diffusion. Burch and Winsor conclude that the water that escapes through the skin of a subject resting quietly in a comfortable environment is water that has diffused through the skin and not water that is secreted by the underlying sweat glands. It is suggested that the terms "insensible perspiration" and "sensible perspiration" are not specific enough and that the terms "diffusion water" and "sweat" should be employed.

HISTOPLASMOSIS IN MAN. ROBERT J. PARSONS and C. J. D. ZARAFONETIS, Arch. Int. Med. **75**:1 (Jan.) 1945.

Histoplasmosis for many years was believed to be a rare tropical disease, but during the past decade the disease has been found widespread in the United States and in widely scattered places throughout the world. Darling characterized the disease as one in which there are irregular fever, emaciation and splenomegaly. Small encapsulated organisms resembling Leishman-Donovan bodies can be found in the tissues, particularly in the cells of the reticuloendothelial system.

Parsons and Zarafonetis review 56 cases of histoplasmosis which have been mentioned or described in the literature and 15 cases which at the time of this review had not yet been published. They state that of the 61 cases on which there were sufficient data for analysis, some form of cutaneous lesions were present in 19 (ulcers in 9, a papular eruption in 4 and purpura, usually occurring in the last two or three days of life, in 6). Petechial hemorrhages and bullous lesions were each noted once. Chronic ulcers sometimes occur in the center of the papular lesions. The ulcers are frequently deep, with sharp, steep edges, giving a punched-out appearance. Of the 15 cases which they add to the literature, only 3 presented neither oral nor cutaneous manifestations. In 3 there was ulceration of the tongue; 1 presented ulceration of the mouth and palate; in another there were granulomatous lesions of the mouth, lip and nose and in another there were oral granulomatous lesions and also a nodule in one auditory canal. There was also 1 instance of a generalized papular eruption, which may have been due to concomitant Hodgkin's disease.

TWO CASES OF MORVAN'S SYNDROME OF UNCERTAIN CAUSE. HARRY PARKS and O. S. STAPLES, Arch. Int. Med. **75**:75 (Feb.) 1945.

In 1893 Morvan first described 7 cases of painless infections of the hand. He recognized the association with disease of the spinal cord, which in most subsequent cases has been proved to be due to syringomyelia, with trophic lesions an outstanding feature. Parks and Staples describe 2 cases in which the diagnosis of syringomyelia seems improbable, the fundamental disease apparently being an unusual neuropathy of undetermined origin. They state that the first symptoms are sensory and usually consist of absence of pain with burns or other injuries. Later there develops loss of the sensation of pain, temperature and usually touch in the distal parts of all four extremities. Trophic changes soon become prominent in the form of ulcers, atrophy of the bones and changes in the nails; spontaneous amputation of small parts becomes necessary by reason of infection. The course of the disease appears to be relatively benign. The authors contrast the neural changes with those of syringomyelia, and conclude that it is a rare disease which warrants further study.

FATAL PANNICULITIS. NATHAN B. FRIEDMAN, Arch. Path. **39**:42 (Jan.) 1945.

Although a number of cases of nodular nonsuppurative panniculitis have been recorded, reports which include postmortem observations are rare. This patient

died of staphylococcic septicopyemia and not of panniculitis as such. The ulceration of subcutaneous nodules which occurred in the case is not usually present in panniculitis, but this feature has been described in an occasional report.

LYNCH, St. Paul.

MANAGEMENT OF CHANCROID IN A TROPICAL THEATER. E. M. SATULSKY, J. A. M. A. **127**:259 (Feb. 3) 1945.

The diagnosis in 1,555 cases of chancroid was made on clinical grounds alone after laboratory procedures were used to eliminate complicating diseases, particularly syphilis. The best criterion in the differential diagnosis of chancroid remains the clinical appearance of the lesions. The cutaneous reactions are at best of confirmatory value and do not alone suffice to establish a diagnosis. In cases in which there were soft, fluctuant, suppurative inguinal lymph nodes incisions and drainages were not performed. The pus was aspirated with a syringe through a cannula. After all the pus was evacuated, 1 to 1.5 cc. of 7 per cent tincture of iodine was instilled into the cavity. Sulfathiazole was found to be the most efficacious drug to be administered orally. One gram (15 grains) was given four times a day for five days, followed by 0.5 Gm. (7½ grains) four times a day for ten days. The average hospitalization in all cases was 11.2 days.

BLOOD AND SPINAL FLUID TESTS FOR SYPHILIS IN MALARIAL PATIENTS. HAROLD W. POTTER, LEWIS H. BRONSTEIN and CHARLES M. GRUBER, J. A. M. A. **127**:699 (March 24) 1945.

One hundred consecutive patients hospitalized for malaria had blood and spinal fluid taken within forty-eight hours of entrance to the hospital. These patients had no history of syphilis. The Wassermann reaction of the spinal fluid was negative in every case. Twelve per cent of the men had positive blood reactions, and an additional 10 per cent had doubtful reactions. It appears that the factors which produce the biologic false result in the blood are not present in the spinal fluid. All patients had had at least one test for syphilis on entry into the army. Physicians should be wary of making the diagnosis of syphilis from only one test in a patient who has had malaria. The authors confirmed the observation of Moore, Eagle and Mohr that serums that are positive with less sensitive tests and negative with more sensitive ones are probably not syphilitic.

BULLOUS DERMATITIS (DERMATITIS MEDICAMENTOSA) FROM PENICILLIN. GEORGE E. MORRIS and JOHN G. DOWNING, J. A. M. A. **127**:711 (March 24) 1945.

A man received 1,000,000 units of penicillin for a postoperative infection. Four days after the last injection the patient noted itching of the left hand and arm, and twenty-four hours later erythema and edema of the left hand, arm and left side of the body appeared. On the sixth day after penicillin had been injected there was tense pitting edema of the entire hand and forearm. These parts also showed erythema and multiple ruptured and unruptured bullae, filled with clear, thin, yellow fluid.

EPIDERMAL AND DERMAL SENSITIZATION EXISTING IN THE SAME INDIVIDUAL. HARRY J. TEMPLETON, J. A. M. A. **127**:908 (April 7) 1945.

Cases of epidermal and dermal sensitization from drugs, plants, foods and autogenous products are reported. Combined epidermal and dermal sensitization may occur from allergens reaching the skin from without or from within. Primary sensitization has nearly always occurred from allergens applied to the surface of the epidermis. The dermis may be sensitized to exogenous materials that have penetrated unchanged through the epidermis to reach the deeper layers, or the dermis may be sensitized to inflammatory products formed in the epidermis consisting of a union of the offending externally applied allergen and the tissue protein

of the epidermal cells. The most frequent of these combined sensitizations are those resulting from topical application of drugs, particularly the sulfonamide compounds.

CONTROL OF SYPHILIS IN PREGNANT WOMEN UNDER THE CARE OF THE GENERAL PRACTITIONER. HERMAN M. SOLOWAY, J. A. M. A. **129**:500 (Oct. 13) 1945.

The plan of treatment of pregnant women provided for a weekly intramuscular injection of heavy metal without interruption throughout the term of pregnancy and eight to ten weekly injections of an arsenical drug with an occasional rest period of four weeks. The scheme of treatment was so arranged that the arsenical drug was administered in the last weeks of pregnancy. There were normal nonsyphilitic children in 94.31 per cent of the 550 cases in which treatment was started before the end of the fourth month of pregnancy. In 83.58 per cent of the 134 cases in which treatment was begun before the end of the fifth month of pregnancy, there were normal nonsyphilitic children. In 409 cases of syphilitic pregnant women placed under treatment after the fifth month, 50.6 per cent terminated in the birth of normal nonsyphilitic children. In 355 cases of syphilitic pregnant women in which no treatment was given, 26.48 per cent terminated in the birth of normal nonsyphilitic children.

THE TREATMENT OF CARDIOVASCULAR SYPHILIS WITH PENICILLIN. RALPH E. DOLKART and GEORGE X. SCHWEMLEIN, J. A. M. A. **129**:515 (Oct. 13) 1945.

It was necessary to discontinue penicillin therapy for 2 patients with syphilitic aortitis because of the untoward effects noted. It has been shown that there is a rapid involution of syphilitic lesions with penicillin therapy. When cardiovascular syphilis is treated by intensive methods, frequently a therapeutic paradox occurs.

HENSCHEL, Denver.

STUDIES ON LYMPHOGRANULOMA VENEREUM. HELEN JONES, GEOFFREY RAKE and BARBARA STEARNS, J. Infect. Dis. **76**:55 (Jan.-Feb.) 1945.

The authors found that at blood levels of 1.4 to 5.8 mg. per hundred cubic centimeters, sulfadiazine, sulfaguanidine and sulfathiazole are the most active, sulfanilamide less so and sulfapyridine least of all. Increasing the blood level of the drugs to a point below that which is lethally toxic does not per se decrease mortality but actually increases it, because of combined disease and toxicity. Although death is prevented by sulfonamide therapy, most of the mice used in these studies became sick. This disease may merge imperceptibly into the symptoms resulting from chronic hydrocephalus.

Carriers of the agent are common in surviving mice. Without further therapy the rate falls steadily until at the end of about a year a fairly constant level (approximately 30 per cent) is reached. Increasing the level of the sulfonamide drug in the blood at the time of infection decreases the carrier rate. The carrier rate can also be decreased by a course of sulfonamide therapy several weeks after the initial infection. At this time, in the absence of acute disease, high blood levels of sulfadiazine may be employed without lethal toxicity. Carrier strains recovered from mice show changes in virulence and resistance to sulfonamide compounds. Two of nine strains showed decreased virulence and one increased virulence. Four of eight showed definite increase in resistance to sulfonamide drugs.

Sulfathiazole is active in vitro. As with bacteria this action in vitro is completely virucidal only when high concentrations of the drug are employed. With lower concentrations delay in development of infection occurs. This suggests that some of the infective units had been inactivated or that all had been damaged sufficiently to delay further development on removal to a favorable environment or that both processes were at work. In such studies of activity in vitro by subsequent inoculation into chick embryos it is essential that one remove as much of the drug as possible before inoculation, since small amounts introduced into the embryo will influence the results.

CORNBLEET, Chicago.

LYMPHADENOSIS BENIGNA CUTIS: CLINICAL AND PATHOLOGICAL STUDY. B. BAFVERSTEDT, Acta dermat.-venereol., 1943, supp. 2.

An attempt is made to classify and clarify the confusing situation which exists with respect to a group of tumors of the cutis and subcutis which are composed of lymphoreticular tissue and characterized by a benign course.

In the past, two types of such tumors have been differentiated: (1) Spiegler-Fendt sarcoid and (2) lymphocytoma. Bafverstedt is of the opinion that the classification should be revised and that tumors described under these two headings constitute one entity. He suggests a new term for this widened conception, "lymphadenosis benigna cutis."

On the basis of this new classification, materials from 41 cases were studied, and a review was made in respect to clinical appearance, histology, etiology, pathogenesis, differential diagnosis, treatment and prognosis of this disease.

Lymphadenosis benigna cutis attacks persons of all ages and occurs two to three times more frequently in women than in men. The tumors involving the cutis and adjoining parts of the subcutis are bluish red and vary in size from small nodules to tumors of the size of a closed fist and plaques several times as large as a man's palm. These lesions may disappear spontaneously, sometimes leaving atrophic scars.

Two forms of the disease can be distinguished: (1) isolated tumors which may appear in several localized regions and (2) multiple disseminated tumefactions. The former occur in persons of all ages and are most common on the face, lobes of the ears, nipples and scrotum. These are slow growing and seldom recur after treatment. The latter, which are comparatively rare, attack older persons and appear in several regions of the body simultaneously. The tumors in this form are large and deep and have a protracted course and a tendency to recur.

The tumors are made up of reticuloid and lymphocytic cells in a thin argentophile reticulum to form a lymphoreticular mass. The reticuloid cells usually predominate. The presence of plasma cells and swelling or proliferation of the fascicular endothelium are constant findings. This is the general picture of lymphatic tissue after slight or moderate inflammation. In these tumors, in addition, polymorphonuclear leukocytes are sometimes present.

The disease is definitely benign. There is no evidence of similar lesions in places other than the skin. There is no change in the normal blood picture. The only change in the hemopoietic system is a mild occasional lymphadenitis. Malignant degeneration has never been demonstrated.

The disease must be differentiated from leukemic or aleukemic lymphadenitis, Malignant degeneration has never been demonstrated.

The cause is unknown, but the author believes that in many instances the disease is a peculiar type of reaction to irritation, which may be pruritus, trauma, an insect bite and, possibly, venous stasis. It occurs occasionally in conjunction with atrophic or sclerosing processes (acrodermatitis atrophicans, scleroderma, cutaneous nodules, and others). The diagnosis, to be other than presumptive, must be made by histologic examination. Examination should include smears of blood and possibly of bone marrow.

The disease must be differentiated from leukemic or aleukemis lymphadenitis, Boeck's sarcoid, lupus erythematosus tumidus, round cell sarcoma and polymorphous sarcoma.

Both varieties are highly sensitive to irradiation. After roentgen ray therapy, the isolated tumors do not as a rule recur. The multiple disseminated type does recur, and no statement can be made as to whether a complete recovery is possible. For the latter type, arsenic has been administered with varying success.

The prognosis as to life is good in both varieties. As to recovery, it is good in the isolated form but doubtful in the multiple disseminated form.

CUTIS RHOMBOIDALIS NUCHAE. F. KOGOJ, Acta dermat.-venereol. **21**:631 (Aug.) 1940.

In a survey of 860 peasants in the mountainous country near Travinik in Yugoslavia, 22.79 per cent had cutis rhomboidalis nuchae, of which 72.72 per cent were over 80 years of age. No cases of its occurrence were observed in persons under 23 years of age. The principal provoking factor is the repeated exposures to ultraviolet rays at an altitude of 800 to 1,600 meters, with the possibility of tar acting as a sensitizing agent. The disease was almost always bilateral; in only 1 case in 196 was it unilateral. Colloid degeneration of the conjunctiva was constantly observed as an associated change. In fact, a diagnosis of cutis rhomboidalis nuchae cannot be made unless the conjunctival degeneration is present. Histologically, there are degeneration of both collagen and elastin and dilatation of the blood vessels. Cutis rhomboidalis nuchae is, in Kogoj's opinion, not a precancerosis, such as farmer's or sailor's skin, but a degenerative atrophy

THE TREATMENT OF VITILIGO WITH INTRADERMAL ADMINISTRATION OF GOLD. K. L. YONG, Acta dermat.-venereol. **21**:657 (Nov.) 1940.

Nine patients with vitiligo and 1 with albinism were treated by injections of a gold compound (lopion). The 9 with vitiligo were treated by the intradermal method, and the albino was treated by both intravenous and intradermal methods. Ultraviolet ray therapy was given to 2 patients and then discontinued when the author decided that it was superfluous. Pigmentation appeared at the site of injection in all the patients with vitiligo, irrespective of subsequent ultraviolet irradiation. The treatment of the albinism was a complete failure, disproving, according to the author, that pigmentation is due to the local deposit of gold in the injected areas. No serious side reaction developed in any of these patients, although a mild scaly dermatitis, which disappeared in one week when treatment was discontinued, appeared at the sites of injection in several patients.

The author concludes that gold somehow stimulates the exhausted melanoblasts in vitiliginous areas and could not possibly help albinos, since in them melanoblasts are totally absent.

CONGENITAL ECTODERMAL DYSPLASIA OF THE ANHIDROTIC TYPE. O. KOALUND-JORGENSEN and J. F. CHRISTENSEN, Acta dermat.-venereol. **22**:1 (Feb.) 1941.

Congenital ectodermal dysplasia of the anhidrotic type is characterized by the absence of sweat glands, deficient dentition, poor development of the scalp hair, saddle-shaped nose, atrophic rhinitis and occasionally the absence of sebaceous and mammary glands.

A review of the literature produced 58 cases, to which the authors add 2 of their own. The patients of the 2 cases described were brothers, children of a consanguineous marriage.

Sections of normal skins were examined microscopically and showed the absence of sweat glands, sebaceous glands and hair follicles.

These patients suffered great discomfort due to the absence of sweat glands, with resulting lack of heat regulation. In hot weather or on exertion, the body temperature became elevated and they suffered from headache and became dyspneic. Any febrile infection made them acutely ill.

In most of the authenticated cases in the literature the disease is familial. In all but 7 cases the patients were males, and it is suggested that, like hemophilia, the dysplasia is inherited as a sex-linked recessive.

ROBINSON, Washington, D. C.

Society Transactions

BROOKLYN DERMATOLOGICAL SOCIETY

David M. Davidson, M.D., *President*

Seymour H. Silvers, M.D., *Secretary*

Oct. 16, 1944

Verruca Plana Juvenilis. Presented by DR. E. ALMORE GAUVAIN.

R. S., a white married woman aged 38, had a few small flat brownish lesions on her cheek seven years ago, after her baby was born. These lesions increased in size and number. There were no subjective symptoms. In February 1944 all warts were curetted off, and their bases were cauterized with iodine. By June all the warts had recurred.

Examination reveals many superficial, rounded and oval, brownish elevations on the forehead and cheeks, varying in size from that of a lentil to that of a lima bean.

The patient is presented for discussion as to therapy.

DISCUSSION

DR. LESSER M. FRUCHTBAUM: I believe that this diagnosis is open to question. The possibility of malignancy should be borne in mind, since the lesions did recur. There is one dark lesion in particular which looks malignant, and a specimen for biopsy should be taken.

DR. DAVID M. DAVIDSON: If one were looking for some complicated diagnosis, one could think of epidermodysplasia verruciformis, but I agree with the diagnosis as presented. I have never heard of verruca plana becoming malignant. Roentgen therapy should not be used in this case.

DR. MORRIS M. ESTRIN: I believe that these are seborrheic keratoses. They did have the suggestive color and appeared larger and softer than those ordinarily seen in cases of juvenile warts.

DR. NATHAN PENSKY: If this is a case of verruca plana, then roentgen therapy is to be recommended.

DR. M. E. GOEBEL: Flat warts disappear with roentgen ray therapy.

DR. LESSER M. FRUCHTBAUM: The diagnosis suggested by Dr. Estrin, seborrheic keratoses, is closest to being correct of any presented here. These warts are not flat, and they will never respond to roentgen rays. I have had a good many patients with flat warts on the face, and such warts clear after three or four exposures to roentgen rays.

DR. JOEL SCHWEIG: I agree with the diagnosis as presented. This disease is an outstanding therapeutic problem. It may prove recalcitrant to any form of therapy; on the other hand, it may clear up spontaneously. To illustrate this, I wish to report a case which has been under my observation. The patient, a youth of 17, was afflicted with juvenile warts on the face and hands for several years. Roentgen irradiation, electrodesiccation, injections of a bismuth preparation and arsphenamine proved of no avail; on the contrary, the disease continued to spread. As a last resort I prescribed protoiodide of mercury in the homeopathic dosage of 1/40 grain (1.62 mg.) to be taken three times daily. Within fourteen days a complete clearance of the eruption occurred. Of course, I did not claim that the last remedy was responsible for the cure. It proves again that *post hoc* is not to be confused with *propter hoc*.

DR. C. THOMAS CHIARAMONTE: I agree with Dr. Schweig that in some of these cases the warts are intractable; by and large they present a rather difficult problem in treatment.

DR. E. ALMORE GAUVAIN: I appreciate the discussion of this particular case. I presented this case tonight for several reasons. First, I had hoped that my diagnosis might be incorrect. When I first saw the patient, in February, I made sure that the lesions were flat warts. On two occasions curettement was done. My previous experience with this type of treatment has been entirely satisfactory. I had used protoiodide of mercury and yellow mercuric oxide locally. When seen in June, she had a full fledged recurrence. I prescribed yellow oxide of mercury. I suspected the correctness of my diagnosis because of the growth of the individual lesions. I have never seen flat warts grow as large as these lesions. After examining one or two of the lesions I thought of the possibility of multiple benign cystic epithelioma, but I could not follow it through. Another reason for presenting her tonight was as part of psychotherapy. My experience with roentgen rays has been unsatisfactory. I have used as many as six doses of 75 r and have not had satisfactory results. Since the diagnosis is generally agreed on, I shall try the protoiodide again.

Malignant Melanoma. Presented by DR. LESSER M. FRUCHTBAUM.

Mrs. A. S., aged 71, presented herself at the clinic of the Long Island College Hospital on Jan. 22, 1940, with an oval lesion of one week's duration, the size of a pea, which was of a dark color and ulcerated and situated on the right leg about 4 inches (10 cm.) above the ankle joint. The clinical diagnosis was infected pigmented nevus or pyogenic granuloma. On January 27 the lesion was removed by surgical diathermy, and the report on the section was that the lesion was a pigmented nevus or a malignant tumor. The lesion healed after several months. On July 6, 1942 the patient returned with a dark blue lesion of six months' duration, which appeared at the periphery of the scar of the former lesion. Microscopic examination at that time showed a malignant melanoma. The lesion was destroyed by desiccation. On August 31 the patient again appeared, with a dark bluish raised lesion of one week's duration, the size of a small pea, at the upper pole of the old scar (the first lesion). It was removed by desiccation. On March 22, 1943 there appeared a dark spot in the center of the scar of the first lesion, which was removed by desiccation. On June 14 the patient returned with a few small, black lesions of three weeks' duration, located at the periphery of the old scar. They were removed by desiccation. The histologic examination showed that the lesion was either a pigmented nevus or a malignant neoplasm. On March 27, 1944 a new bluish lesion, the size of a pea, appeared at the periphery of the former lesion. This too was destroyed by desiccation. On July 24, after the lesion had healed, a new pinpoint blue spot appeared at the periphery of the old scar. On September 11 a large infiltrated lesion, the size of a quarter, appeared in the center of the old scar. By September 25 this mass had increased in size.

On October 9 physical examination showed a granulomatous mass in the center of the old scar. The examination tonight shows a mass the size of a small walnut situated in the center of the old scar. The tumor mass is hard and deeply infiltrated and raised above the level of the skin; it has a raw surface, is uneven and discharges a serosanguineous fluid.

To summarize: The initial lesion appeared about five years ago and recurred after each destruction. It has not metastasized, and the patient is in good health. The histologic studies of several biopsy specimens showed a malignant melanoma.

DISCUSSION

DR. E. ALMORE GAUVAIN: I doubt the accuracy of the histologic diagnosis. I do not believe that a patient with a malignant melanoma would survive after the tumor had been tampered with. I think that this lesion is a pigmented nevus. If there

is a recurrence of the primary lesion, there should be a more radical excision at the secondary operation, more and more being excised and the excision being deeper and wider.

DR. SEYMOUR H. SILVERS: It is difficult to make a histologic diagnosis on the basis of a clinical examination. Clinically, the lesion is an epithelioma. I think that even a malignant melanoma may remain inactive for many years.

DR. DAVID M. DAVIDSON: The patient is naturally too old now for radical treatment. Besides, she has enlarged lymph nodes now. However, when the diagnosis of malignant melanoma was first made the entire lesion should have been removed by a wide excision.

DR. ABRAHAM WALZER: This lesion should have been excised in its entirety originally. Electrodesiccation should not have been done. At the present time the patient has palpable nodes. I still think that the proper treatment, in spite of her age, would be to excise the entire area extensively.

DR. LESSER M. FRUCHTBAUM: I presented this case for two reasons: first, because this type of lesion is rare, and second, because physicians do not generally have patients under observation over such a long period as in this case. At the time the patient first appeared, the lesion was small. I believe that I did a thorough job of excision by surgical diathermy and that there was no justification for the removal of the leg in a person of her age. When the lesion recurred one and a half years ago, it appeared at the periphery of the old scar. Apparently I should have removed more than I did at that time. Each time I performed electrodesiccation, not excision as had been done the first time, and I destroyed at least ½ inch (1.3 cm.) of healthy tissue beyond the lesion; I felt that if I could thus control the spread of the lesion, without resorting to radical measures, that would be justifiable. What one sees tonight is a new lesion. It is a real fulminating tumor, and it does not clinically resemble a melanoma. The patient feels well and has not lost weight, and the question that still remains is what to do further—shall one amputate the leg or leave the patient alone?

Circumscribed Scleroderma. Presented by DR. LESSER M. FRUCHTBAUM.

I. H., aged 12½ years, presented herself at the Unity Hospital with lesions of four years' duration on her abdomen. These lesions are large oval-shaped plaques, about 2 inches (5 cm.) in diameter, symmetrically distributed on either side of the lower part of the abdomen. The lowermost lesions are white in the center, infiltrated, leathery on palpation and surrounded by a violaceous ring. The uppermost lesions are violaceous and purple and are not infiltrated. The lowermost lesions developed first. There are no subjective symptoms.

The Wassermann reaction of the blood was negative. Examination of the urine showed no abnormalities. A blood count was within normal range, and the basal metabolic rate was —15 per cent.

DISCUSSION

DR. DAVID M. DAVIDSON: This case is interesting, inasmuch as a similar case presented last year by Dr. Silvers elicited considerable discussion. Some members did not believe that soft patches like the ones the patient presented could be scleroderma, while others thought that the eruption was scleroderma but in the stage of involution. The patient presented tonight has hard and soft patches and states that the soft patches are the young lesions and all the hard patches were soft originally and only later became hard.

DR. C. THOMAS CHIARAMONTE: Some years ago I presented before this society a patient with scleroderma without infiltration. At that time, the case provoked considerable discussion because of its lack of infiltration. This patient presents lesions which have the typical sclerodermatous changes and other lesions which are smooth. The latter lesions are slightly pale and have a bluish red, sharply

defined peripheral zone. I believe that one is fortunate in seeing this eruption tonight because it links the so-called smooth scleroderma, described by Gougerot, with true scleroderma.

DR. LESSER M. FRUCHTBAUM: Most patients with scleroderma are female. The ratio is 2 to 1, and in a good many cases the basal metabolic rate is lowered. I have given this patient thyroid. At present the lesions are circumscribed, but they tend to spread more and more.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

Dr. John L. Fanning, *Chairman*

Dr. Frances M. Keddie, *Secretary-Treasurer*

Oct. 20, 1944

A Case for Diagnosis (Sarcoidosis?). Presented by DR. FRANCES A. TORREY.

L. H., a 28 year old white woman presented from the department of dermatology, University of California, was first seen in the dermatology clinic on Oct. 9, 1944.

At that time she had a tender subcutaneous swelling deep in the medial aspect of the right leg, which, she says, has been growing gradually for five to six years.

Examination reveals a dozen or more painless subcutaneous nodules scattered over her body. Many of these, she says, have been present for a long time. She discovers new ones from time to time. She says that her brother has similar nodules.

There is a patchy hyperpigmentation on the forehead and to a lesser degree on the face, and it has been increasing for the past year.

The patient has noted a feeling of increasing fatigue for the last six months.

The results of the physical examination were essentially normal.

The roentgenograms of the right leg revealed a mass in the right calf, with periostitis involving the cortex of the adjacent bone.

DISCUSSION

DR. MERLIN T. R. MAYNARD, San Jose: I think that one might be just as well dealing with a case of lipomatosis. The diagnosis can be established only by removal of one or several of the nodes for study. Lipomatosis is more probable as sarcoidosis is a rare possibility.

Tuberculosis of the Skin. Presented by DR. FRANCES A. TORREY.

E. W., a 44 year old Negro woman presented from the department of dermatology, University of California, was first seen in the dermatology clinic on Sept. 5, 1944.

At this time she has several bean-sized subcutaneous nodules in the supraorbital and infraorbital areas of the right eye, over the area of the left antrum, one nodule in her right forearm and another nodule above the right elbow.

There are crusted granulomatous lesions on the alae nasi, and the hypertrophic injected mucous membrane of the nose almost obstructs the nasal outlet on both sides.

Granulomatous nodules are also present in the conjunctivas, with some mucopurulent discharge. All these lesions have been present for about a year.

The physical examination gave no further information.

The blood and urine were essentially normal. The Kolmer and Kahn reactions were negative. The basal metabolic rate was +11 per cent. Tuberculin tests of the skin (in dilutions of 1 : 1,000 and 1 : 10) elicited negative reactions. Roentgenograms showed a normal chest. Biopsy specimens of the nasal mucosa showed tuberculous granulation tissue; a nodule from the elbow showed lipomatous tissue.

DISCUSSION

DR. NORMAN N. EPSTEIN: I think that this case has not been completely investigated. One of the nodules apparently was not of a tuberculous nature. They are in unusual locations. The one on the cheek does not suggest tuberculosis. Apparently the patient has a tuberculous process on the nose. However, histopathologic studies of one of the nodules on her face should be made.

DR. MERLIN T. R. MAYNARD, San Jose, Calif.: Since she hails from Texas, I think that it would not be a bad idea to perform a coccidioidin test and to search slides for Coccidioides immitis.

DR. ROBERT STEWART: In respect to coccidioidomycosis, of course, Coccidioides should be looked for in any case of granuloma. Coccidioidomycosis cannot be ruled out by performing a coccidioidin test on her. Of course, there are other observations to be reported before a definite conclusion can be made as to whether this is sarcoid or true tuberculosis. Inoculation of a guinea pig is indicated.

Xeroderma Pigmentosum. Presented by DR. FRANCES M. KEDDIE.

J. A. B., a white woman aged 53 years, has had pigmentation of the face, neck, arms and legs since the age of 9. Numerous epitheliomas and keratoses on the arms and face have been treated by excision, cautery and roentgen rays over a number of years. The skin is dry, with pigmented macules, telangiectasia and keratoses on the exposed area.

There is no familial history of similar diseases of the skin. Her parents were not related. Two sons, aged 23 and 29, are not affected.

DISCUSSION

DR. MERLIN T. R. MAYNARD, San Jose: I agree with the diagnosis. One fact I should like to point out is that in the résumé it is said that there is no familial history of the disease. The patient, however, stated that one of her sisters has had exactly the same manifestations. She is seven years younger than the patient and has had the disease just as long as the patient has had it. I think that this helps to substantiate the diagnosis.

DR. NORMAN N. EPSTEIN: The disease is rarely seen in a woman the age of this patient. Most of my patients have been children, and they rarely survive to this age. It seems that she has only a moderate degree of sensitivity to sunlight. I was interested to note that in xeroderma pigmentosum the epitheliomas are frequently of the basal cell type. I had the impression that they are usually of the squamous cell type. This woman, however, has had both.

DR. B. V. A. LOW-BEER (by invitation): Some of the lesions—including one under the eye, as I remember—were treated with roentgen rays. There was another, a huge lesion on the cheek, which was treated with radioactive phosphorus. The two responded equally well to the treatment. I had as a patient a young girl, sent to me by Dr. Hiram Miller, with the diagnosis of xeroderma pigmentosum. She had an epithelioma under her left eye and many others all over her body. Many of the lesions were treated before she came to me. She is 20 years old and has had the disease process since the age of 5 or 6. Her father and mother are cousins. In order to study the sensitivity to various wavelengths we tried radiation with a wavelength of 2,500 angstrom units. I wish I knew what to do for this girl.

DR. FRANCES A. TORREY: As I remember, some of the lesions were not epitheliomas; some were angiomas.

DR. B. V. A. LOW-BEER (by invitation): Yes, and some were hyperkeratoses. One was a huge ulcerating lesion which was treated with 100 kilovolt roentgen rays. I gave her about 4,500 r.

DR. REES B. REES: The patient under discussion lacks all symptoms of photophobia, which is an almost invariable accompaniment of xeroderma pigmentosum beginning early in childhood.

NOTE.—This patient later gave the following family history: Her sister, at the age of 55, with brown eyes, fair skin and light freckles, has had a few tumors removed from the face; a half-brother (same father), at the age of 40, is not affected. Her mother died from the results of an accident at the age of 26. Her father is alive and well at the age of 73; he has black hair and eyes. Her paternal grandfather died at the age of 84; her grandmother died at the age of 20 from a cause not known; her grandmother's sister died at the age of 30 and was thought to have had a condition similar to that of this patient. No information was obtained about maternal relatives.

A Case for Diagnosis (Eczema? Simulating Leprosy). Presented by DR. JOHN GRAVES.

S. L., a 49 year old Chinese man presented from the department of dermatology, University of California, was first seen in the dermatology clinic on Oct. 11, 1944. His complaints were of induration, thickening, lichenification and pigmentation of the face and hands.

April 1943 was given as the date of onset of the disease. Despite much local therapy there has been little or no improvement. Itching is a prominent and constant symptom.

The Wassermann reaction was negative.

Allergy studies are now being conducted, and the probability of a contact allergy (vegetation) is suggested by Dr. Albert H. Rowe. A son and a daughter of the patient are said to suffer from hay fever.

DISCUSSION

DR. OTTO E. L. SCHMIDT: One must also consider the ropy enlargement of the ulnar nerves in this patient. I think that it is compatible with what one sees in leprosy. The hypertrophy of the face looks unlike the chronic excoriation of eczema. I think that hypertrophy of the tissues and subcutaneous tissues as well can actually be seen.

DR. PAUL FASAL: It seems to me that the nodules on his ear lobes are suggestive of leprosy, and I think that they should be examined thoroughly.

DR. MERLIN T. R. MAYNARD, San Jose: I think that the texture of the skin itself speaks against eczema. Lichenoid reactions always have a rough scaly surface. This man's skin is soft. I could not feel any lichenification. I think that it is probably a case of leprosy simulating eczema.

DR. FRANCES A. TORREY: I think that histologic examination would settle the diagnosis.

DR. REES B. REES: A further point is that the lesions are chiefly confined to the exposed areas.

NOTE.—Acid-fast bacilli were not found in scrapings from the nasal mucosa or in sections of tissue removed from the forehead.

Dermal and Ocular Pemphigus. Presented by DR. PAUL FASAL.

F. B., a white man aged 65, first seen on Oct. 8, 1944, presented a generalized vesicobullous eruption on the entire skin, palate, buccal mucosa, tongue, pharynx and anus. His general condition was poor. He gave a history of arthritis deformans of about ten years' duration. His cutaneous lesions had started around his mouth several months earlier and spread gradually. On Sept. 10, 1943, he was admitted to the department of dermatology of the University of California Medical School, with a diagnosis of pemphigus, and he remained there until September 23.

On Oct. 11, 1943, internal medication with solution of potassium arsenite U. S. P. was started, with 1 drop three times a day, this being increased every fourth day by 1 drop until 7 drops three times a day were given. Then the dosage was decreased in the same way. After about ten days of this medication the fresh blisters, which still formed daily, seemed to be smaller. On October 25, there was

a severe eruption of large blisters on his trunk. Ten days later great improvement in his skin and general condition was noticed, and within five more weeks his skin had healed completely.

In March 1944, there was a relapse, with vesicobullous lesions all over his skin but not on the mucous membranes. Another course of solution of potassium arsenite was started. The cutaneous lesions again subsided gradually, and there has been no severe relapse since, except for occasional small blisters. Both eyes were affected when the patient was seen first. The ocular condition was diagnosed by Dr. P. Dolman as pemphigus. While he was receiving arsenical medication, the patient's skin healed but his eyes became gradually worse. At present the patient's skin shows only pigmentary changes from previous lesions; both eyes are badly damaged.

DISCUSSION

DR. NORMAN N. EPSTEIN: There is no question about the diagnosis in my mind. It seems that I have seen more benign forms of pemphigus recently in elderly people as well as in middle-aged people. I do not believe that this is because of the therapy. These patients have remissions just as if they were spontaneous and not related to therapy. One patient was given penicillin, 1,000,000 units, without any effect whatsoever on the pemphigus. I still think that vitamin D therapy seems to do something that other forms of therapy do not. It is more satisfactory in general than anything else that I have tried. This patient has done remarkably well.

DR. PAUL FASAL: I did not think that in this case improvement after arsenicals was coincidental, but of course it is possible. The patient had had vitamin D before, without apparent effect.

Hydroa Estivale. Presented by DR. OTTO E. L. SCHMIDT.

J. M., a 12 year old Mexican boy, presented from Stanford University School of Medicine, complains of an eruption on the face present since 1938.

The birth and development were normal. Cod liver oil by mouth caused his face to become flushed. His father has hay fever.

The eruption began on the face and the backs of the hands as papules which became vesicular during July and August each year, especially on exposure to sun. For the remainder of the year the papules persisted.

He entered the pediatrics outpatient department in August 1942. A provisional diagnosis of allergic eczema was not substantiated by extensive cutaneous tests.

Physical examination revealed a palpable thyroid gland and dermographia. On the entire nose, malar regions and eyelids are closely grouped erythematous papules and vesicopustules. The lower lip is edematous, dry, red, scaly and fissured. A few papules are present on the backs of the hands.

On Sept. 13, 1944, biopsy of a specimen from the eyelid showed an intraepidermal vesicle filled with polymorphonuclear leukocytes and necrotic debris. In the corium was a focal round cell infiltration and some fibrosis.

The hemogram and results of examination of a timed urine specimen and of urinary porphyrin content were normal. The Wassermann reaction was negative.

There has been some recent improvement following protection from sunlight.

DISCUSSION

DR. FRANCES A. TORREY: I thought that the lesions were perhaps more characteristic of lupus erythematosus than of hydroa estivale. As I understand, the latter usually clears during the winter and the lesions leave decided atrophy.

DR. WILLARD M. MEININGER: When the patient was first seen, he was much worse. The eruption looked a good deal more like lupus erythematosus. I had not seen him for several weeks until this evening. The improvement is most likely due to the fact that winter has just begun. Histologic examination was done to help with the diagnosis; the observations were not characteristic of lupus erythematosus.

DR. OTTO E. L. SCHMIDT: Various possibilities have been considered. As I understand, many people classify hydroa estivale in two groups, depending on the presence or the absence of porphyrinuria. In the cases in which there is abnormal porphyrin present, the lesions are apt to be large and leave scars. In the cases without porphyrin the patients often have smaller lesions, which may persist even through the cold weather and which usually do not produce scars. This type of disease disappears with the attainment of adolescence and leaves little or no trace of the former process. The histopathologic structure is typical of hydroa estivale and shows epidermal vesiculation. The sweat glands are not primarily involved, as is found in granulosis rubra nasi.

DR. MERLIN T. R. MAYNARD, San Jose, Calif.: I agree with the diagnosis. I should like to say that I have known instances in which this disease persisted during the winter months. At the last meeting of the American Dermatological Association in San Francisco, there were several patients who had hydroa estivale but did not have porphyrinuria. These cases were typical examples of hydroa estivale. The case which is presented tonight is not typical of lupus erythematosus despite the concentration of the lesions on the nose. The lesions are entirely too vascular and active for lupus erythematosus. The eczematous-like patches which weep and heal with scars are more typical of hydroa than of lupus erythematosus.

Dermatitis Herpetiformis. Presented by DR. PAUL FASAL.

A. H., an 8 year old white girl, has had a generalized vesicobullous eruption for the past seven months. A few vesicles appeared on the legs following a sore throat. When first seen, in March 1944, her extremities were covered with vesicobullous lesions from the size of a pinpoint to that of an egg. The lesions arose from a normal skin and were extremely pruritic. New vesicles continued to develop until the trunk, face and scalp were covered. Many of the lesions on the trunk were grouped.

Her general health is good. There is no history of medication prior to the onset. Use of iodized salt was discontinued in March.

The white blood cell count was 19,000, with an eosinophil count of 15 per cent. Contents of the vesicles were sterile.

Medication with sulfonamide drugs produced toxic reactions of malaise, fever, urticaria and albuminuria. Solution of potassium arsenite U. S. P. was not tolerated. Acetarsone, 0.125 Gm. twice daily, was taken by mouth from April to July 1944. Until September there were several relapses, characterized by the eruption of large bullae. Lately there have been no large blisters, but every four to five days crops of fresh small blisters appear on the trunk, neck or extremities. There have been no lesions on the visible mucous membranes.

Physical examination reveals nothing abnormal save for the skin and the hypertrophic tonsils. This patient was vaccinated in the fall of 1943.

DISCUSSION

DR. MERLIN T. R. MAYNARD, San Jose: It is of particular interest to me to see this patient tonight because during the last three months I have seen 2 children with this disease. In 1 it developed soon after vaccination, and she died as the result of the disease three weeks later. The other child is in Children's Hospital. It is worth while to take a look at her. It is said that the eruption came on five weeks after a tick bite. I do not know whether the tick bite had anything to do with it, but she had definite pemphigus. I gave this child penicillin, and the lesions cleared completely. When penicillin was stopped and sulfathiazole was given, there was a relapse. She had almost universal lesions. This child is likely to die also from the way the disease is going. I am much interested in the relationship of vaccination in 1 case and tick bite in the other. I suggest that this is a virus disease possibly of the type of foot and mouth disease, as has been suggested in the past. It is suggested that since the tick is a vector of the virus causing the

disease in cattle and vaccine is the vector of a similar virus there is possible correlation between the 2 cases.

DR. NORMAN N. EPSTEIN: This case is clinically one of dermatitis herpetiformis. The lack of constitutional symptoms and the type of lesions suggest strongly dermatitis herpetiformis.

DR. FRANCES A. TORREY: I want to report 1 case which I have been following. I was able to keep the patient fairly clear with sulfapyridine, 2 Gm. a day. I had to administer this for over a year. He is now fairly well and comfortable by taking 300 mg. of nicotinic acid and 15 mg. of pyridoxine a day.

DR. JOHN L. FANNING, Sacramento: I have a boy who has remained well for about a year by taking 1 Gm. of sulfadiazine a day.

DR. PAUL FASAL: I believe that Dr. Maynard's suggestion regarding smallpox vaccination in relation to the disease should be considered. I know of several cases in which the disease started in children shortly after vaccination for smallpox.

Fox-Fordyce Disease. Presented by DR. NORMAN N. EPSTEIN.

G. R., a married woman aged 37, about one year ago noticed an itching eruption of the axillas and the suprapubic area. The disease has remained stationary, without relief of symptoms during this time. Menstruation began at the age of 13 and has been regular. There have been no pregnancies. Except for a general nervousness, she has had no complaints other than the pruritus.

The results of a physical examination were normal. A thorough endocrine examination by an internist, Dr. Minnie Goldberg, revealed no endocrine imbalance except a mild hypothyroidism. No evidence of ovarian dysfunction was noted.

A laboratory investigation was noncontributory. Biopsy revealed dilatation of the sweat glands, with a slight inflammatory reaction around them. Because Fox-Fordyce disease has been linked with disturbed ovarian function, Dr. Goldberg first gave her male sex hormone (methyl testosterone) 5 mg. sublingually daily. This caused an aggravation of the symptoms. She was later given estradiol benzoate, 2.5 mg., by injection weekly. There has been no definite response to five such injections.

Dr. Goldberg recommends that a combination of gonadotropic and estrogenic therapy be tried.

DISCUSSION

DR. OTTO DIEDERICH, Fresno: There is no question about the diagnosis. I should like to suggest the use of estradiol benzoate ointment. I have had experience with it in 2 cases, and it helped considerably.

DR. NORMAN N. EPSTEIN: I have nothing to add, except that the patient seems to be a little better tonight than she was the last time I saw her. Perhaps the therapy is beginning to work, despite the fact that the internist was rather discouraged about it.

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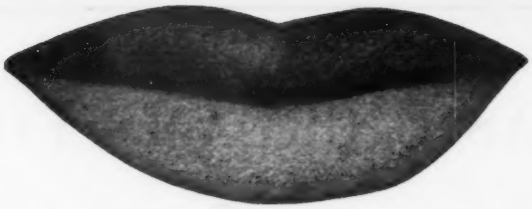

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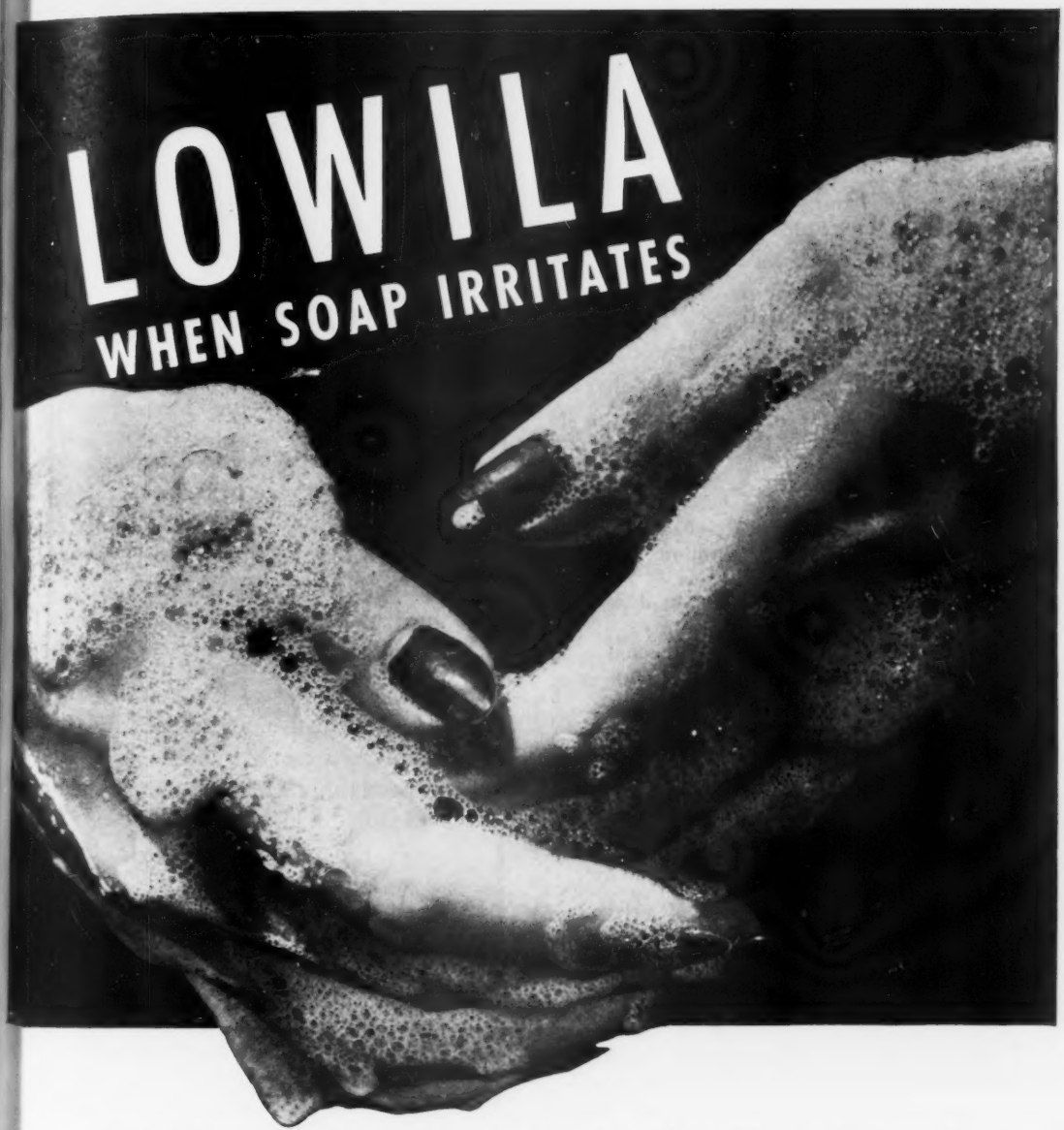

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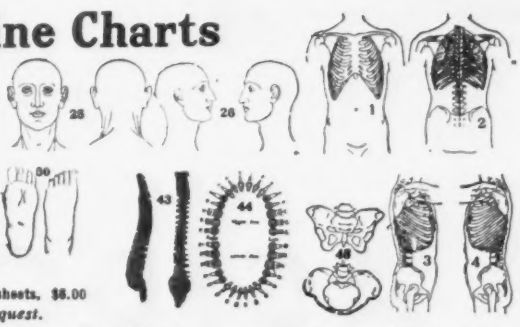

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